BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY FEBRUARY 24 1945

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY FEBRUARY 24 1945

THE HUNTERIAN MUSEUM: YESTERDAY AND TO-MORROW*

BY

G. GREY TURNER, LL.D., D.Ch., M.S., F.R.C.S.

Hunter will stand out for all time not only as a famous surgeon-pathologist but as one of the first of the great exponents of the experimental method in medicine. The circumstances of the times imperatively dictate that attention should be paid to the story of the other great record which he left to posterity in his collections. This task coincides with my own inclinations, for I have been attracted to museums from my earliest days, and indeed it seems as if the desire to collect had come so naturally as to be almost inborn. There are some who question the value of medical museums or consider that they have become superseded now that the art of book illustration has been carried to such a high state of perfection. Before we go on to consider the huge task of restoring our museum this point of view requires some consideration, for to those of us who so much appreciate museum collections it seems unnatural. When contrasted with even the most precise and beautiful picture the actual specimens seem so much more real: their size, contour, and perspective are so different from anything shown on a flat surface. But the great advantage is that they can be handled, looked at from all aspects and from new angles. Further, it is possible to re-examine them by dissection, to cut them up if necessary, and to review their minute structure by histological methods.

How Hunter was Inspired to Collect

John Hunter's teachers doubtless had their own preparations, and although I can find no account of Cheselden's collection there seems no reason to think that he would be behindhand. Bart's, always to the fore among the medical schools, is fortunate in that its history has been so carefully compiled by Norman Moore, and in his great work appears the following record by the Governors of St. Bartholomew's Hospital under date of June 23, 1726: "Two convenient rooms were prepared under the cutting ward—one for the more decent laying of the dead patients before their burial, the other as a repository for anatomical or chirurgical preparations." This repository would later contain the treasures of Percivall Pott, and a specimen of a congenital hernial sac with the original roll of paper which Pott placed through the neck not only survives but is still used for teaching nearly 200 years after it was prepared. But undoubtedly the chief stimulus was William Hunter's collection, which was well started before John made that notable journey from Scotland to join his brother as assistant in the dissecting-room. William Hunter in his lecture syllabus always set great store on his preparations, and in it referred to the making of these and undertook to teach the processes in his anatomy course.

Before we go further into the circumstances which inspired John Hunter to build his museum we ought to know something of his fascinating life story. It is with his boyhood that I want especially to deal, for his early years were said to have been wasted in idleness, and it was constantly held against him that at 17 he could neither read nor write and that part of his youth was spent in a carpenter's shop. In after-life John spoke of those early years spent in the country around his home as of special value in cultivating his powers of observation. In retrospect I think we must recognize that the time spent in close touch with nature was probably among the most valuable in the whole of his life. Like most small boys, Hunter was inquisitive and was always wanting to know the reason for the things he saw about him. Doubtless he had much time to wander about and make observations and to think, but I cannot believe that he was entirely idle. In Scotland in those days there were few who could be, for it was essential that everyone should work for his daily bread. The family was in straitened circumstances, and we may be sure that John not only helped his mother but was employed about the business of their holding. The life of the farmyard must have been thought-provoking, from the traditional query, Why does water run off the duck's back? to Why do fowls sometimes eat their feathers and sows devour their young? Pigeon-lofts infected with contagious tumours, crop-bound fowls, lambs with grass-ill, and "sturdy" sheep, all provide fascinating problems. The accidents to which stock are liable would arouse keen interest in the surgery of injuries and repair, and would certainly teach a reverence for the healing powers of nature. The vagaries of swallowed foreign bodies, like the fate of a needle and thread swallowed by a kitten and discharged from an abscess in the neck when death seemed inevitable, would also be an arresting experience. What lad could ever forget seeing a young horse trailing its intestine on the grass after castration, and what inquiries might it stimulate in after-years in connexion with the anatomy of congenital hernia? Quite possibly the more thoughtful men about the place cut up dead animals in the hope of finding the answers to some of these questions, and thus Hunter would learn the wonders of the disclosures of post-mortem examinations. Life about small farms runs close to nature, and household gossip would often be intimate. The phenomena of reproduction and abortion and obstetric emergencies of all sorts obtrude themselves wherever stock-breeding is part of a hard-won livelihood, and it is interesting to recall that in later life Hunter envisaged artificial insemination. Family illness and episodes of the crises of human fate would often be discussed, and in the Hunter household death was all too familiar. At about 18 it was felt that something should be done to help him to make a career, and he went to Glasgow to assist in the workshop of his brother-in-law, a cabinet-maker. There is no record of how John's time was actually employed, but he probably learnt many lessons not only in using his hands but in conduct, and it would probably be obvious to him that application and industry are the only roads to success. After two years his brother-in-law failed in business and John returned to the old home. Some who have commented on Hunter's later career have rather looked askance at this period in the cabinet-maker's shop and have suggested that he might have been better employed. With this I would join issue, for I believe that a period working with tools, and especially the clean precise tools that wood-workers employ, is an excellent education for anyone destined to use his hands for his life's work.

One of my earliest teachers and colleagues, the late W. G. Richardson of Newcastle-upon-Tyne, was an amateur cabinet-maker who could turn out wonderful work. But with his big clever hands Richardson was also an expert dissector after the true Hunterian style, and some of his preparations were very beautiful. He had the further gift of being able to convey what he saw to paper, and many of the drawings which illustrate his essay on the prostate

* Some extracts from the Hunterian Oration, delivered at the Royal College of Surgeons on Feb. 14, 1945.

could scarcely be bettered. Withal he was an expert surgeon, and I have never seen anyone who could carry out a better radical breast operation.

When John returned home from Glasgow wanting an outlet for his activities he was armed with the attributes of a training in observation, disciplined hands, and an inquiring mind. At that time William, in London, was sending letters home describing the fascination of his work in the great city and extolling the opportunities it provided. We may depend upon it those letters would often be read and discussed in the family circle. Most probably it was John's mother who wrote to her elder son asking him if he would do something for his young brother. Doubtless John felt a secret pride in William's success, and probably needed very little persuasion to undertake that journey to London in search of fame and fortune. Once in London, William's influence and example must have had a very powerful effect on his younger brother. William was not only a very successful teacher of anatomy but was a fashionable practitioner in midwifery, courted by the best people and popular among them. Withal he had a passion for collecting. He knew the art of the *préparateur*, which he first learnt from Douglas, to whom he had been apprenticed, and which was later furbished on his Paris visit. His preparations were among the best in London, and the museum he founded was generally regarded as one of the finest then in existence, being very readily accepted by the University of Glasgow after his death.

Inception and Growth of his Collection

It is often wondered where John Hunter secured his specimens in his early days, for it has been stated that while working as demonstrator for his brother any preparations he put up were placed in William's museum, and we know that several prepared by John are in the Hunterian collection in Glasgow. It is highly probable that, like other keen young men working in dissecting-rooms, he might remove some portions that were of special interest and take them to his lodgings to dissect in private; or he might hoard up some treasure, surreptitiously hidden away until such time as he felt he could use it. In these days, when the operating theatres so constantly supply the needs of our museums, it is perhaps forgotten what a wealth of pathological conditions is unearthed in the dissecting-rooms. It is recorded that Hunter collected when with the Army in Belle Isle, and when he came home in 1763 he was supposed to have something like 200 specimens of normal and diseased structures. In the Golden Square days he was mostly concerned with studies in comparative anatomy, and his great sources of supply were the animals that died in the menagerie then kept in the Tower. He never lost an opportunity of acquiring anything that would make a suitable preparation. Some were presents from friends. "If you will step in at Banks' in Soho Square, you will find the corpse of the fine Sierra Leone cat, the inside of which is at your service. The skin is to be stuffed for the British Museum." So wrote his friend Sir Joseph Banks, who was later President of the Royal Society and always his firm supporter. Other friends were roped in to help, and his old pupil Jenner was an unending source of supply. Further specimens were secured by purchase, and we know, in connexion with the skeleton of the Irish giant, to what length of monetary impropriety he was prepared to go rather than lose some specimen on which he had set his heart.

Hunter's Method of Work

The making of his preparations, the actual labour of creating his museum, must have been a colossal task, and there can be no doubt that the major part of this work fell on Hunter himself. Just think of the dissections, the macerations, the injections, and the display of the pathological material! Then there were the jars to choose and the specimens to be suspended or otherwise displayed, and the tops to be fixed. There were no ground lids to be cemented, but each jar had to be covered with pig's bladder or parchment, which had to be securely tied on; and after drying there was the outer cover of thin sheet-lead to be fitted, secured, painted, and probably varnished. Hunter certainly knew all about these processes, as we may gather from his remark concerning his brother-in-law, young Home, who was told that his damned clumsy fingers were all thumbs and that he would never have sense enough to tie down a bottle. Doubtless he would get help from those about him and from his pupils, but his was the master hand, and indeed he was probably the only one who knew anything about the art of preparation. Hunter himself was taught to make preparations during his apprenticeship to his brother and there can be no doubt he made it a hobby and soon learned to excel. But, even if he did enjoy the work, the time involved must have been enormous. Anyone familiar with the dissection of animals, and especially large ones, will know what a long time it takes: Clift speaks of Hunter standing at his work for hours. The same applies to pathological specimens, for they must be prepared, displayed, and set up when fresh to get the best results. Then there is always the recording to be done, descriptions to be written, labels to be fixed, and other duties of the kind. There is evidence that Hunter was concerned with all these tasks.

Most of his experiments were done at Earl's Court, but the arrangements of his establishment there showed that rooms for dissection were not forgotten and that the work of making preparations was provided for. It was there that he had the large copper for boiling bones; and we have the story of how the body of O'Brien, the Irish giant, was taken there in the dead of night and hastily dismembered, and the parts boiled so that the skeleton could be quickly prepared rather than risk detection if the slower process of maceration was employed. Just think what it meant to be engaged in the active work of preparation almost every day for a period of 30 years. Hunter's routine was to rise at 5 a.m. or earlier in summer and 6 a.m. in winter, and to go at once to his workroom, where he remained until breakfast-time. Certain it is that these morning hours were spent in association with those about him, for it is recorded that on the very morning that he met his end he was particularly happy among his pupils. In one branch of his museum work he was not particularly careful, and that was the labelling of jars and the recording of dates. But Hunter was deeply conscious of the need for a careful record, and it was only the difficulty of applying some method in the stress in which he lived that allowed this delinquency to occur. No one, however, can say that Hunter was not systematic. He was constantly making notes on odd bits of paper, and these were all carefully sorted and entered up into his record books; but he was not careful about dates. He was also a great letter-writer and kept his correspondence carefully.

The Workroom

Hunter's dissections and museum work were done in his own house, for there were no laboratories or workrooms kept for him at the hospital, and he had to provide all that he required and to supervise everything that went on. At each of his homes arrangements were made so that he could fulfil these self-imposed tasks. There was undoubtedly good accommodation at Earl's Court, but the question of transport had to be considered. This was by coach, and it is interesting to ponder on the loads that Hunter's coach must have carried to and fro in those busy days when it had to be a sort of covered wagon taking all kinds of human and animal remains from London out to the country and back. The methods of specimen-preparing that were used at that period are worth considering. There were the ordinary dissections, some of them very delicate and some of great size. Many of these were mounted in spirit. Because of the difficulty of securing jars large enough and a sufficiency of spirit, some were prepared by the dry method. His original collection contained over 500 of this type. It was a tedious method, for the specimens had to be very carefully cleaned, and packed or distended with air; they were then painted with an arsenical preparation and hung up until dry. Finally they were carefully varnished and re-varnished, and as a rule mounted in jars to protect them. Specimens made in this way will often last for many years, and there are still some Hunterian preparations of this kind in good condition. Then there were the injected specimens—a method in which Hunter excelled and for which he left directions—but they do not appear to have conveyed the secret of the art to those who have tried to follow in his footsteps. Corrosion specimens were also used. A great many of the pathological preparations were in spirit, which meant a lot of work for their proper display and the fixing of the jar covers.

The dry bone specimens had all to be macerated or boiled—both slow processes—to get the best results. There were also the calculi, the plants, foreign bodies, and the fossils, of which Hunter left so large a collection.

A great deal of Hunter's work must have been done in artificial light provided by candles. Heating must have been a difficulty, for there was nothing but open grates, which would probably burn coal. Judging by my boyhood experiences in the North, it is highly probable that in winter some of the fires would never be allowed to go out—not only for the purpose of heating the house but because it was the only method of securing a ready supply of hot water from a kettle on the hob and of obtaining a light. Clift mentions that Hunter made spills from the scraps of letters on which he had previously made notes. Matches as we know them were not introduced until 1834, and if there was no fire it would be necessary to use a flint and steel with tinder-box to strike a light. Cold water may have been conveyed through pipes to a basin or sink in his workroom, for it is interesting to observe that among Hunter's belongings sold by auction after his death were two leaden cisterns. The question of the disposal of waste must have been rather troublesome, for there was no water-carriage system, and dry closets and cesspools for the convenience of so large a household would require frequent emptying. Fortunately soap was plentiful and cheap, but after a heavy day and an evening spent in an atmosphere rendered grimy by a succession of smoky candles, there was no hot bath for Hunter before he retired to bed in the early hours of the morning. For his literary work there were only quill pens, as shown in Reynolds's portrait. His handwriting is good and legible but occupies a considerable amount of space, and we know that during those very full evening hours he filled an enormous number of notebooks. During the latter years of his life he dictated a good deal to an amanuensis, but there is no evidence that any sort of shorthand was employed. The manuscripts which were taken away from the Castle Street house to suffer so sad a fate at the hands of his brother-in-law, Everard Home, were said to fill a coach. Fortunately for us a considerable number were not destroyed. Hunter's dissecting and other instruments were of good quality.

With what we should consider to be such inconveniences there were bright features, for Hunter was saved the tyranny of the telephone and long out-of-town journeys. Had he done nothing more than care for his museum, his pupils, his lectures, his writings, and supervise his amanuenses and artist he would have been very fully employed and would have accomplished a great deal of which he might be proud. But these were really only side-lines, for he conducted a very large practice. His professional work began immediately after breakfast, when he saw patients at home. It is said that those waiting were so numerous that they often invaded his wife's drawing-room. At a fixed hour he left home in his coach to make outside visits and for hospital practice, and he never delayed his departure even if persons of importance were still waiting to be seen. He did not return home until four o'clock, which was then the usual dinner hour; after dinner he commonly slept for an hour on a couch in what was called the afternoon bedroom. Then began what must have been some of the most strenuous work of the day—letter-writing, case-recording, the description of his dissections, and the task of laboriously turning out those literary works which eventually made for him a fame which has been lasting. In addition, for years he lectured at his own house every alternate evening from April to October. Can we assume that he was so intensely occupied and so absorbed in the practice of his profession that he found no time for affairs around him? No one could have been more single-minded or more absorbed in his pursuits. Assuredly he scorned delights, and certainly no one has ever lived more laborious days.

The Disaster and After

On the night of May 10, 1941, the College Museum was struck by a heavy high-explosive bomb and showered by incendiaries. As a result the greater part of the Museum and some parts of the College were destroyed, and about two-thirds of our collections vanished in the conflagration. The story of the measures which had been taken from 1938 onwards to guard against such a tragedy, the details of the disaster, and the steps taken to salvage and care for what remained of our treasures has been admirably told by Prof. A. J. E. Cave, the Assistant Conservator, in the Scientific Reports of the College for 1939–40 and 1940–1. It is a sad chapter in College affairs, and has caused much regret and unhappiness to lovers of the great museum we so much treasured. Clearly our duty is to look to the future and to consider plans with ways and means for complete restoration.

The Future

The disaster has not only imposed a greater responsibility than ever before but has provided an opportunity of which it is necessary to make use. After some months of hard work the Museum Committee was able to present to Council a suggested plan for the restoration of the Museum, together with many ideas on future developments. The Museum will be reborn in circumstances different from those which existed when it first came into being over 130 years ago. Then there were no museums devoted to anatomy and pathology in this country, and only one or two London hospitals had a few preparations for the use of their pupils. Now all medical schools up and down the country have museums, some of them excellent, so that from the purely vocational aspects of medical education the country is well provided. But there is a large floating body of students in London, mostly Empire students not owing allegiance to any school in the Metropolis, who naturally look to the College for museum facilities and who must be catered for. Other museums, and notably the natural history collections at South Kensington, are now in a position to carry out many of the activities previously shouldered by the College in the field of zoology and natural history, and others may be expected to develop—for instance, in anthropology.

Broadly, the conclusions of the Museum Committee, accepted by Council and by the Hunterian trustees, are that the museum should be restored and built up around the surviving collections to illustrate the development, structure, and functions of man, together with the accidents and diseases to which he may be a victim, with such reference to the animal kingdom as may help to elucidate the problems involved. The part of our museum that earned us an international reputation was the physiological and comparative anatomy series. In any event that would be the part most difficult to replace and, alas! it has suffered severely. The restoration of the pathological sections will be much less perplexing. One of the first questions that had to be settled by the committee was how to dispose of the surviving Hunterian preparations. The first inclination was that they should be kept together as a precious relic and a memorial to the work of our founder. The idea of having a room set aside, as a sort of shrine, in which they might be exhibited together with any other Hunterian relics, was most attractive and made a strong sentimental appeal. But more mature reflection convinced us that this would not be in keeping with the Hunterian tradition, and that it would be much better to have them allocated each in its proper section of the general collection, where they might act as a leaven and a stimulus. No one would wish to claim that all the Hunterian preparations are now of great value; some have served their purpose, their usefulness having been superseded by advances since Hunter's day, and some are so deteriorated as to be of little but sentimental value. Others were classical and some unique, and some possibly guarded secrets of nature which up to the time of their destruction had not been divulged. Those most interested and best able to judge agree that, so far as possible, destroyed Hunterian specimens with a lesson to teach or recognized as classical or potentially valuable should be replaced. An idea very much in my mind is the suggestion that when the specimens can be safely returned to the College an exhibition of the whole surviving Hunterian collection should be set up in one of the rooms together with all the existing relics of Hunter that can be got together. This should be attractively set out according to the original plan, and should be on view for several months, so that those who are interested may have the rare privilege of seeing assembled together what remains of the collection. Photographic and other records should be made, and these would serve in years to come to interest those who had not enjoyed the opportunity of seeing such a unique exhibition.

Among many who have talked about the restoration of the museum there are not a few who dread that the new museum will be cluttered with animal skeletons. There are some who have no use for the wonders presented by the bony framework of the elephant, the giraffe, or the whale, and no veneration for extinct monsters like the Irish elk or the megatherium. They may be astonished to hear that it was never the policy of the College to collect such taxonomic exhibits, but those that came to us in various ways were not rejected. But if a skeleton or part of a skeleton, irrespective of its size, is necessary to display some feature in comparative anatomy or physiology which leads to the better comprehension of the structure and function of man, then let us hope it will be preserved and exhibited. The same general principle should apply to the soft parts of animals, however large or however minute. Just fancy the interest of comparing the oesophagus of the giraffe with its insignificant counterpart in man! Perchance the secret of achalasia may be disclosed in the study of its neuro-muscular mechanism. Then how truly awe-inspiring to be able to re-create Hunter's wonder when contemplating the enormous aorta of the whale. And what bearing may the structures of that great creature yet have on the understanding of some of the problems of aeronautics? It is the intention to keep the museum up to date as a collection by replacing deteriorated specimens and by constantly adding better ones as these become available. Only the very best obtainable should be found on our shelves. But there is another point, and that is the question of the history and after-history of the cases from which specimens have been obtained. Many a poor-looking specimen is valuable because of its clinical history, and many another grows in value as the long after-history of the case adds to its interest and importance. The renewal and follow-up department must be much more active than ever before. Personally, I would like to see the day when it would be a distinction to have specimens accepted by the College because of their excellence and the complete histories with which they were accompanied. Specimens should be accepted and retained only because of their value, and the days are long past when the distinction of the donor could claim precedence over the distinction of the gift. Special collections should be accepted only with the proviso that the specimens may be dispersed among the general collection if this is considered best in the interests of the museum.

Another idea I want to bring forward is the value of special but changing exhibits. The restored museum should possess a large demonstration room where special exhibits could be put up from time to time and kept on display for a month or more. A section on the anatomy of approach is somewhat of a new idea, and would be intended to display the anatomy of operative incisions. How often has the novitiate wondered exactly what are the structures encountered and to be divided or thrust aside in carrying out the exposure of the kidney, excision of the rectum, or the exposure of the Gasserian ganglion? For each operation a series of special dissections would have to be available and alternative routes of approach would have to be illustrated. I am convinced of the value of such a plan, and am most interested to find that it was employed by James Douglas, who died in 1742, and who is remembered by the peritoneal pouch to which his name is linked. The section of general pathology was of the greatest value, embodying as it did the very kernel of the Hunterian idea. This should be restored in its entirety, and there may be directions in which it could usefully be extended. The old museum contained the most remarkable collection of calculi—about 1,000 in number—of all sorts, which were classed mostly according to the parts of the body in which they were found. In the future museum, considerations of the formation of calculi—calculus disease—should provide a more thought-provoking section. Then there is the idea of group exhibits where the ravages of any one condition are shown together irrespective of the number of the regions of the body that may be involved. A medico-legal section is very badly needed, for there is none of any moment in a public museum, and it would seem a very proper activity for us to undertake. I was very much impressed with such a collection in Buenos Aires, in which most beautiful wax models were largely used to supplement the exhibits.

Gynaecology and obstetrics were always well represented in our museum, but the specimens might well be brought more in line with present-day knowledge. There is no branch of surgery which lends itself better to museum illustration, and there ought to be no difficulty in rebuilding our collections and in making them second to none. The odontological collection was fortunately spared. Under the devoted guidance of its honorary curator, Sir Frank Colyer, this branch of surgery which originally owed so much to Hunter, was very worthily represented. Each of the special senses must have sections devoted to its exhibition, as in the past, but this must not prevent certain conditions being included in the section of general pathology or elsewhere if some principle can thereby be the better illustrated. In view of the well-directed activities of the Wellcome Foundation I think we might properly restrict our historical collection to relics of Hunter and his immediate associates. A large part of our surgical instrument collection has survived, and might well form the nucleus of an exhibit to illustrate their evolution and development. Sections for venereal disease, anaesthesia, blood transfusion, and wound treatment would appear to be necessary, and will certainly prove useful and interesting. A standard collection of the very best *x*-ray films should not be excluded from such a museum as we have in mind. The results of surgical intervention—i.e., the after-results of operations—should be fully illustrated, and might form an increasingly fascinating exhibit. Similarly the results of experimental surgery should be demonstrated by specimens. Of the thousands of experiments carried out, how little in the way of museum records is available. In other ways there should also be a closer association between the department of experimental surgery and our museum. Another good feature which must be continued and developed was the annual show of new specimens, always on exhibition in connexion with the Annual Meeting of Council in July.

In order that we may help serious workers to extend knowledge it will be necessary to have a large amount of store material, not merely tucked away, but easily accessible and properly catalogued or indexed. Facilities should be provided for its close examination, even if dissection is necessary. The use of such material could not be very open-handed, and only accredited workers who seriously wanted to obtain information which they could not get elsewhere should expect to be allowed such facilities. I also have in mind proper study rooms, where those engaged in a particular piece of work could keep their specimens and could work on them without necessarily having to reassemble their material each day. For some years there has been much talk of research in the profession, but this has usually been in terms of laboratory work and usually animal experiments. Many people forget how much research is waiting to be done in other directions, and there is certainly a great deal that might be carried out in any well-equipped museum. It is especially important that we should provide for the very many keen young surgeons who are working in and about London, and they should be encouraged to make use of the opportunities for study which our museum affords. We should aim at making our collections the most famous in the world, but we must not assume that other museums have stood still, and it is most important that we should have information as to what may be going on elsewhere, so that inquirers might be helped by direction to the proper quarter; for this and other purposes a museum bureau would be most useful.

Conclusion

Hunter's saying, "Why think; why not try the experiment?" has been handed down as a sort of tradition; but to look and see and to verify everything by observation is to carry out the same fundamental principle, which is so revealing that its recognition fully justifies the existence of our museum. Everything that we can learn about Hunter encourages the re-creation of the very best museum that can be assembled. We want it to be a Mecca for inquiring students from every part of the world. Its reconstruction will be slow; it must be patiently done, and it must be thorough. We must plod on and on till the task is well under way, knowing full well that it can never be completed. There is always the example of Hunter's driving force to encourage us, for "there were no drones in his hive."

INFLUENZA EPIDEMICS AND THE INFLUENZA VIRUSES

BY

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LECTURE II

In my first lecture I attempted to outline the history of influenza epidemics in this country in recent years and to describe the characteristics of the human disease invoked by the influenza viruses. In the present lecture I wish to refer mainly to the study of immunity to the viruses under natural or experimental conditions and to the development of possible methods of control of influenza.

Immunity to Influenza Virus Infection

From the earliest days of work with influenza virus in the laboratory the subject of immunity and of artificial methods of producing resistance to infection has been given constant attention. Much has been learnt; much probably remains undiscovered. The ability to control conditions and to standardize procedure in the laboratory has resulted in the accumulation of a valuable body of knowledge of immunity in experimental animals, much of which is probably applicable to the more complex immunity in man. Most of this work has been carried out on virus A, but there is no reason to suppose the results do not apply to virus B also. More recently, however, experiments on human volunteers have been carried out, with the result that knowledge concerning the duration of immunity and the effectiveness of various methods of immunization in man is accumulating rapidly.

Immunity in Experimental Animals

Ferrets are especially suitable for studies of immunity because of the resemblance between the infection induced by the viruses in this species and that occurring in man. Immediately after an attack of the disease the ferret is completely immune to reinfection, antibodies are present in high titre in the serum, and the immunity is broad-based so that heterologous strains of the same major type are resisted in addition to the homologous one. There is even, in the days of early convalescence, a cross-immunity between swine influenza virus and virus A, though not between virus B and virus A. Heterologous cross-immunity of this type may be present, though antibodies to the heterologous strain may not be detected in the serum. As time passes the homologous antibody level begins to fall and susceptibility to reinfection returns. However, homologous antibodies are still demonstrable in the serum when reinfection is possible, and the second attack, though accompanied by fever and nasal symptoms, is usually less severe and is not followed by the development of lung lesions if a lung-adapted strain of virus is used for the reinoculation.

In an attempt to illuminate the apparent failure of antibodies—that is, of humoral immunity—to explain the phenomena observed in the ferret, Francis and I (1938a, 1938b, 1938c) studied the histological changes in the nasal mucosa following primary inoculation and reinoculation with virus A. We found that a cycle of events occurs in the respiratory portion of the nasal mucosa during primary infection. The ciliated epithelium undergoes complete necrosis, leaving only a single basal layer of flattened cells, and, after three days, repair by growth of a many-layered pseudo-stratified type of epithelium sets in. Ciliated epithelium is not re-formed until a fortnight to three weeks after infection, but by the fourth week the damage to the epithelium has been largely repaired. The stratified epithelium present for several days during convalescence interested us very much, and we were able to show that this modification of the normal nasal mucosa, which is present, when immunity is at its height, is resistant not only to reinoculation of virus but to unrelated physico-chemical agents. Zinc iontophoresis or simple instillation of zinc sulphate intranasally in normal ferrets produced an acute necrosis of the epithelium very similar to that of influenza, and repair and regeneration followed a similar course. The ferret convalescent from influenza showed, in the second week, a complete resistance of the nasal mucosa to destruction by iontophoresis, and the epithelium revealed no histological changes after this operation. As the epithelium of the convalescent animal became more normal, destruction by ionization again became possible, until at four weeks a normal reaction was obtained. The converse experiment of ionization of the nose followed by instillation of virus gave, however, no evidence of resistance by the regenerating epithelium to the virus.

These studies demonstrated to us that virus infection was followed by morphological changes, which were of a temporary character only and were therefore inadequate by themselves to explain the observed immunological phenomena. There seemed to us to be an analogy to the experiments of MacNider (1937) on the morphological changes of fixed tissue cells in the liver and kidney resulting from damage by chemicals. Whereas chemical tolerance to those agents was found by MacNider to be accompanied by a permanent modification of the liver and kidney structure, our abnormal nasal epithelium, on the other hand, was only transitory, and with the reappearance of a normal epithelium the non-specific resistance to damage was lost.

The nasal mucosa of ferrets exposed to reinfection at a time when immunity from the first infection had waned underwent necrotic changes similar to those seen in the first attack. Differences were discerned, however. Areas of epithelium sometimes remained normal, so that the necrosis tended to be focal in type, a more rapid repair followed the necrosis, and often the epithelium was not reduced to a single basal layer by the reinfection. This appeared to indicate a conditioning of the nasal mucosa by the first attack, so that the infecting agent was more readily repulsed and the damage more speedily repaired. Furthermore, if the ferret had had two previous nasal infections a solid immunity to a third or fourth inoculation might be encountered and then the nasal mucosa showed no histological changes at all. We studied the antibody levels of some of these ferrets prior to reinoculation, and were led to believe that the actual titre of circulating antibodies at the time of the immunity test was of fundamental importance.

These studies also afforded some explanation of the reaction observed in the ferret after subcutaneous inoculation with the virus. It has already been mentioned that infection does not follow introduction of virus by this route, and though antibodies subsequently develop in the serum the animal is not immune to nasal instillation of the virus, though possibly resistant to the more delicate test of contact infection (Smith, Andrewes, and Stuart-Harris, 1938). If parenteral inoculation of virus is given to a ferret in a state of waned immunity following an actual attack, the immunity may be boosted once more and a solid resistance to a second intranasal inoculation of virus may result. The production of a state of immunity by the re-installation of a high antibody level in an animal whose nasal mucosa is conditioned by previous infection can be readily visualized. Also from experiments on the immunization of ferrets, Francis (1939) was able to show that a considerable quantitative relationship existed between the degree of immunity following subcutaneous vaccination, the level of circulating antibodies at the time of the immunity test, and the amount of virus which was given in the vaccinating dose. Artificial immunization in the ferret is thus dependent for its success on the amount of actual virus antigen which is introduced parenterally; but the susceptibility of the nasal mucosa to infection, aided perhaps by the remoteness of the epithelium from circulating antibody in the serum, makes it impossible to reproduce the complete immunity which follows nasal infection.

Immunity in mice appears to be less complicated than that in ferrets, and it is also easier to produce a state of complete immunity by artificial immunization. The changes in the lung following intranasal inoculation with virus A have been studied by Oakley and Warrack (1940) and correlated with the presence of antibodies in the serum. The production of actual lung lesions was found to be essential with mouse-adapted strains of influenza virus for the subsequent development both of antibody and of immunity. Immunity developing after intranasal infection was broad-based, and was effective against heterologous virus A strains even in the absence of good levels of antibody against such strains. Other observers have found it to be possible to obtain immunity after intranasal infection

of mice in the absence of lung lesions, but only, however, if the virus used is not of mouse origin. Thus Burnet and Clark (1942) showed that unadapted human virus would both immunize and produce antibodies even though no lung lesions were produced, and Eaton and Beck (1940) obtained immunity without lung lesions by using ferret virus or tissue culture from chick embryos.

Because mouse-passage strains of virus must be used in high dilution if the production of lung lesions is to be avoided, it seems that these results simply mean that the effectiveness of immunity after actual infection in mice is closely dependent on the quantity of virus which has actually been administered. The immunity following parenteral inoculation of mice with virus preparations has been closely studied. Inasmuch as massive doses of living virus have to be given intraperitoneally (Rickard and Francis, 1938) in order to produce infection of the lungs by this route, the results of parenteral inoculation with living or with inactivated (formolized) virus are rather similar. Antibodies are most rapidly produced, however, after the introduction of living virus intraperitoneally, and persist somewhat longer than when inactivated virus is used (Oakley and Warrack, 1940). The results of repeated inoculation with either virus preparation are better than those of a single dose. The influence of the subtle changes of past infection in mice is well illustrated by the fact that although antibodies to heterologous strains of virus A are poorly developed after either parenteral or nasal introduction of virus, the immunity to heterologous virus following parenteral immunization is much more feeble than that following actual infection. Eaton and Pearson (1940) noted that about 10 times as much virus was needed to protect against heterologous strains as against homologous ones after intraperitoneal immunization either by living or by inactivated virus. Eaton (1940) also estimated that, given by the same route—that is, intraperitoneally—about 30 times as much inactive virus was needed to produce the same degree of immunity as active virus. The importance of the amount of actual antigen in the production of an immunity which is broadly based and effective against heterologous strains is thus clear. The superiority of immunization based on an actual infection, even if this is inapparent, is also obvious. Two further factors have been shown to operate adversely in the case of parenteral immunization. The presence of foreign protein from the host species used to prepare the vaccine has an interfering action on the effect of the vaccine in stimulating antibody formation, and the intraperitoneal route of inoculation is more favourable than the subcutaneous one (Andrewes and Smith, 1939).

Many of these facts which have been elicited from studies with mice have a bearing on human immunization, as we shall see later. Meanwhile, it is necessary to mention the effectiveness of prophylactic administration of immune serum, either from convalescent ferrets or from hyperimmunized rabbits or horses, in the influenza virus infection in mice. Laidlaw, Smith, Andrewes, and Dunkin in 1935 showed that serum given intraperitoneally saved life and diminished the extent of lung lesions if given either before or after intranasal infection. More recently, others (Henle, Stokes, and Shaw, 1941 ; Taylor, 1941b) showed that the serum was much more effective as a prophylactic if given intranasally, and that some effect was demonstrable even up to 10 days after serum introduced by this route. Trial of the method in ferrets has not, however, given results comparable to those obtained in mice (Zellat and Henle, 1941). Unpublished experiments of Glover and Andrewes, to which I am kindly allowed to refer, indicated that some protection could be given to the lung of a ferret, but that it was not possible to protect the nose by inhalation of atomized serum or by exposure to a coarse spray. The intensity of the infecting dose of atomized virus to which the serum-treated ferrets were exposed was carefully controlled, and even a low degree of immunity was unlikely to have been overlooked.

Immunity in Man

(a) Natural Immunity

At least three mechanisms are now known to be concerned in determining resistance or susceptibility in man to influenza virus infection. The first—namely, the development of antibodies with specific neutralizing power for the virus—has been most studied. The distribution of antibodies to virus A i the population in interepidemic times has been found to b related to age. Children other than newborn babies have leas and adults of middle age have most, antibodies. Cyclic changes in the general level of antibodies in the serum ar correlated with the occurrence of human epidemics in tha levels are highest immediately after an epidemic and lowe before an outbreak, while the individuals with the highe levels after infection undergo the greatest proportional chang with the passage of time. Some individuals, particularly tho in the middle range of antibody levels, possess remarkabl stable antibody titre over periods of many months. Com plement-fixing antibodies also undergo cyclical changes, b are at their highest levels for a shorter period of time aft an epidemic than are neutralizing antibodies. The fact tha sharp changes in titre of antibodies accompanied actua infection and that both clinical and subclinical attacks ar associated with changes of a similar magnitude has alread been mentioned. So far virus has only rarely been recovere from clinical influenza unaccompanied by serological change (Adams, Thigpen, and Rickard, 1944), but it is known fro deliberate infection experiments that clinical symptoms can s times occur without serological alteration, and the significanc of the varying percentage of cases in the various outbreak which yield neither virus nor antibody change (influenza Y can be interpreted in various ways, as previously pointed ou Apart altogether from diagnosis, however, the antibody change during infection are of considerable importance in relation t susceptibility or resistance to attack. All observers are agree that a majority of cases of influenza are drawn from th population group which has the lowest levels of antibody before infection, but that individuals with all levels of antibody yiel cases during an outbreak.

The accumulation of all this mass of information has bee the work of many observers in all parts of the world, an evidence on which these statements are made was fully reviewe by Burnet and Clark in 1942. Our own slender contribution may be referred to briefly. In 1936 Andrewes and I bled a group of 50 medical students at St. Bartholomew's Hospital estimated their neutralizing antibodies, and then observed th experience of this group during the 1937 epidemic. Cases wer scattered through all the various levels of pre-epidemic anti body content, and though we did not prove virus A infectio in all cases, the uniformity of experience in this outbrea indicated the probability of this diagnosis. A large number o cases of influenza B were observed in 1943 and investigate by Hirst's test. There was a fairly marked scatter of case (Chart VII), with antibodies during the acute febrile stage a very different levels. Also, the number of B cases was propor tionately greater in those with low antibody level in the firs specimen of serum. The influenza Y cases whose antibody leve showed no change had on the whole higher levels of antibod than the B cases, but some cases had low levels. The correlatio between the actual multiplication of antibody content in th blood of the B cases and the original content of antibody wa definite, and has been noted by other observers in bot influenza A and B (Chart VIII). It means, as Hirst and other (1942) have pointed out, that the same total quantity of anti body is added to the serum of the various cases, and that th is many times the amount already present in those with lo levels and is relatively less in those with high pre-existing leve of antibody. Comparison between severity of clinical infectio and pre-existing antibody level or degree of multiplication o antibody failed to show any relationship either in virus influenza (Chart IX) or in virus A influenza (Chart X). Th agrees with the known fact that an individual can have subclinical attack or a clinical infection at any pre-existin level of antibody.

One last fact which must be mentioned concerning the ant body response to infection is the degree of change in the seru for heterologous strains of virus. There has been some co troversy between various workers as to whether human respond to infection with antigenically distinct types of vir with the same degree of specificity for homologous strains a does the ferret. The balance of evidence now favours the vie that the amount of antibody in the serum in the acute sta is less when tested against the homologous virus than wh

heterologous virus is used. The actual amount of increase in antibody is also greater for antigenically related than for antigenically distant strains of virus, as our own results (Andrewes, Smith, and Stuart-Harris, 1938) indicated. Magill and Sugg (1944) have recently re-emphasized the importance of this finding in connexion with diagnosis. The existence of a multiplicity of antigenic types of the same major strains during any one outbreak, such as has actually been proved, must also have an important influence on the effectiveness of the resistance of the individual whose antibody titre may be adequate to produce immunity against some but not against other types of virus.

The results obtained from study of human infection indicate that no critical level of antibody exists below which there is susceptibility and above which there is resistance to infection as was thought originally (Hoyle and Fairbrother, 1937; Francis *et al.*, 1937). Burnet (1944) has recently emphasized that the fundamental fact concerning immunity to influenza is that in all recent epidemics never more than 50%, and usually under 20%, of the population experience clinical attacks during an outbreak. It has been shown that cases of actual clinical infection are chiefly drawn from individuals with the lower levels of antibody (Rickard, Lennette, and Horsfall, 1940), but that cases can occur throughout the range of antibodies. Yet the 70-odd% of the population which escapes influenza must include many individuals with low antibody levels, though during the outbreak some—perhaps in widespread epidemics the majority—develop increase in antibodies irrespective of clinical attacks. It is in these individuals that the explanation of antibodies as the chief factor in the resistance to infection breaks down. To what, in fact, do they owe their immunity? Doubtless some escape contact with the virus altogether, but this does not account for those who develop subclinical attacks.

Studies of groups of individuals who have been deliberately infected by spraying with virus A or by inhalation of atomized virus A have given much clearer correlation between antibody levels and immunity than the experience during natural infection (Burnet and Foley, 1940; Henle, Henle, and Stokes, 1943). It appears that standardization of the dose of infection produces clinical attacks only in those individuals with low antibodies in their blood before infection. In the experiments of these workers, 26% and 36% respectively of normal individuals experienced clinical attacks and more developed subclinical infection. In the much more intense exposure to virus B by Francis and others (1944), when clinical attacks were produced in 90% of individuals by inhalation of atomized virus, there was much less correlation with antibody levels. Four months after the original spraying Francis could again produce clinical attacks in 90% of the group sprayed initially, in spite of the fact that they still had an enhanced antibody level as a result of their initial experience. Possession of good antibodies was somewhat correlated, however, with shorter and milder fever. Besides demonstrating the evanescence of human immunity to actual infection by influenza virus, Francis thus showed that the defence against infection could be broken down if the intensity of the infecting dose was sufficiently great. We may perhaps deduce that the intensity of

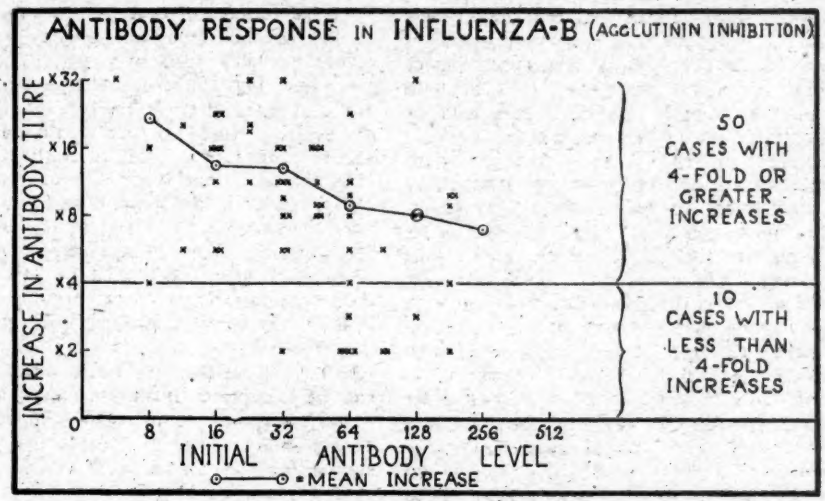

CHART VIII

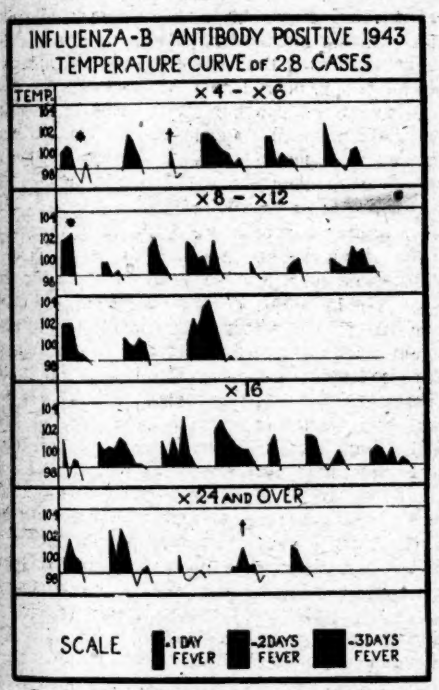

CHART IX.—* Two cases with high initial titre. † Two cases with low initial titre. × 4, etc., indicates the increase in antibody titre (Hirst test).

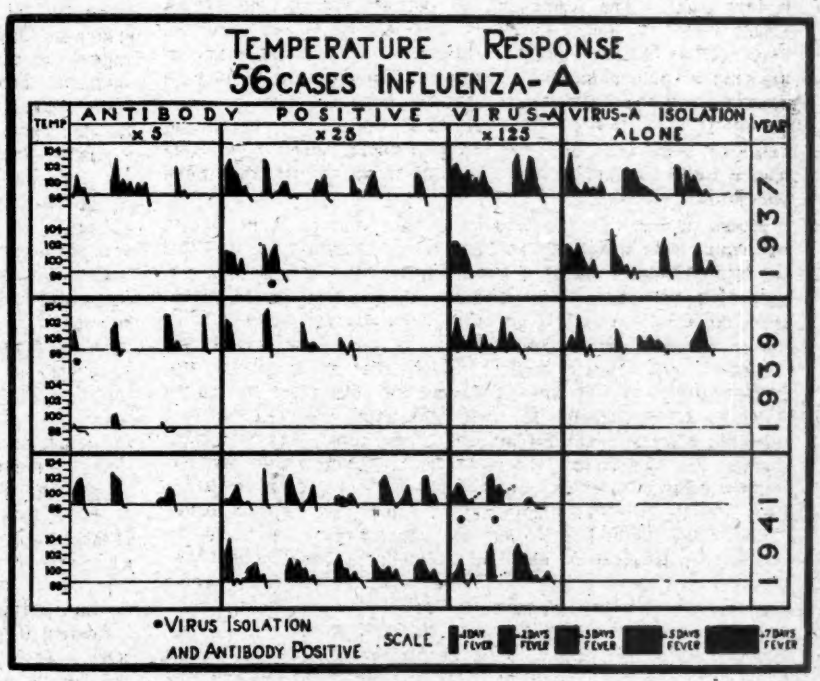

CHART X.—× 5, etc., indicates the increase in antibody titre (mouse neutralization test).

natural infection during an epidemic is much less than that used by Francis and probably less than that of the earlier workers with virus A, in view of the lower percentage incidence of infection observed during natural outbreaks. May it be that repeated exposure to infection during an epidemic breaks down in some individuals the resistance conferred by a high antibody level? Also, may the escape from clinical attack by some individuals with low antibodies be attributed to the fact that they are lucky in receiving just enough virus to cause a subclinical but not enough to cause an overt infection? Other mechanisms governing resistance probably do exist, however, and one of these is the natural defence of the nasal mucosa to attack.

No observations on the changes in the nasal mucosa which accompany human influenza appear to have been made, but a humoral system of defence based on the property of virus inactivation possessed by nasal secretion has been studied both by Burnet and his co-workers (1939) and by Francis (1941). Controversy still exists as to the nature of this substance, which has a wide range of activity against viruses other than influenza. However, different individuals possess different amounts of it, and Francis showed that there was a correlation between the inhibitory activity of the nasal secretion to influenza virus and the influenza antibody present in the blood, and a sharp increase in virus-inactivating power of nasal secretion accompanied infection (Francis and Brightman, 1941). In connexion with this it was also shown (Francis *et al.*, 1943) that an increase in the amount of inhibitory substance in nasal secretion followed subcutaneous immunization accompanied by successful stimulation of antibody production. Burnet, on the other hand, considers the substance to be an enzyme in character, and is inclined now to attribute less significance to its action than at one time (Burnet and Clark, 1942). If, however, both chemical and cellular defence of the nasal mucosa, including the capacity of the nasal epithelium to regenerate rapidly after attack, is considered, it must be obvious that the first line of defence against the virus is probably important. A more doubtful mechanism, which may or may not play a part in the production of clinical phenomena, has been unearthed by Beveridge and Burnet (1944), who studied the skin reactions to inactivated influenza viruses inoculated intradermally. They found that boiled chick allantoic fluid from eggs infected with either virus A or B was capable of eliciting an erythematous skin reaction in both children and adults. No correlation between level of antibody and liability to a positive skin reaction was found, but in children positive reactions were obtained only when possession of some demonstrable antibody suggested past infection or exposure to the virus.

These observations suggested that allergy may be important in determining clinical reaction to influenza virus. Observation on animals has hitherto given little indication that allergic reactions were important. However, Shope and I, in 1938, carried out a few unpublished experiments in which pigs were inoculated intraperitoneally with immune horse or convalescent pig serum and were subsequently inoculated intranasally or exposed to contact infection by swine influenza virus and *Haemophilus influenzae suis*. There was a definite indication that the serum-treated animals were in some way sensitized, because fever and clinical symptoms consistently developed some hours earlier in these animals as compared with the controls who did not receive serum. We were, however, more interested at that time in the possibility of attenuating clinical attacks, and this we failed to accomplish. Allergic reactions in man have been suggested by the deliberate infection experiments of Bull and Burnet (1943), in which symptoms were commoner after intranasal reinoculation than after a first intranasal inoculation with a modified attenuated strain of virus B. An increased incidence of symptoms on reinoculation three to four months after the first spraying of volunteers with the virus occurred in spite of enhanced antibody levels in the serum. The strain of virus used did not produce febrile reactions, and the occurrence of nasal symptoms after both first and second spraying bore no relationship to the subsequent development of an antibody rise in the serum. By the criterion of demonstrable antibody rise, infection was produced in more than 90% of the 23 individuals by the primary inoculation, but in only two instances in the second inoculation. Dissociation of this type between nasal symptoms and immune reaction may be related in some way to the type of infection produced by attenuated viruses, and it was not encountered by Francis (1944) in his reinfection experiments with less modified virus B. Francis, far from demonstrating an increased tendency to symptoms in individuals subject to reinoculation, thought that individuals with the highest antibody titres had less reaction after inhalation of the virus. Time alone will show whether allergy is of much importance in relation to the natural disease.

(b) Artificial Immunization in Man

The discovery of the aetiological agent of human influenza was soon followed by attempts to produce immunity with virus preparations, and these have been actively pursued by several different groups of workers. Emphasis has been largely placed on experiments designed to produce active immunity, and the various workers in this field have concentrated their energies along two distinct lines of attack. British and American investigators have tended to develop methods of immunization based upon the fact that most individuals have, at one time or another, been subject to nasal infection by the virus, and therefore the human problem is essentially one of reinforcing a waned immunity rather than that of developing one in a previously uninfected host. They have therefore tried various methods of immunization by the subcutaneous route, arguing that if a sufficiently intense antibody response could be produced the nasal mucosa could be left to take care of itself. In contrast, Australian workers have concentrated on the development of an attenuated virus strain which could be given intranasally without producing clinical reaction yet producing an effective immunity by reason of its attack on the nasal mucosa, which would be unaffected by subcutaneous inoculation. Such a strain of virus would ideally resemble the yellow fever 17D virus, which has been so successfully used in human immunization against yellow fever (Theiler and Smith, 1937).

Early work in Britain and America was concerned with the demonstration that subcutaneous inoculation of virus enhanced the antibody titres of those inoculated. The fact that inactive formolized virus appeared to be an effective antigen in man was demonstrated at an early date. Furthermore, one inoculation produced as good a rise in antibodies as did several doses. However, detailed study of the factors concerned in determining the relative efficiency of various vaccines in producing antibodies has been chiefly pursued of recent years in America. Hirst, Rickard, Whitman, and Horsfall showed in 1942 that there was a considerable variation in the human antibody response to the same preparation of virus given subcutaneously. The rise in antibodies was correlated with the pre-vaccination titre of the serum, so that the actual amounts of antibody produced by individuals with originally different amounts of antibody were approximately the same as in the case of actual infection. Secondly, the antibody rise induced by subcutaneous vaccination was evanescent and titres had dropped considerably six to nine weeks after vaccination. Thirdly, the antibody response increased in proportion to increase in the amount of virus antigen which was injected. The most concentrated preparations of antigen which were inoculated produced antibody responses of a magnitude similar to those encountered as a result of actual infection. Fourthly, inactive virus, especially in a relatively protein-free medium such as chick allantoic fluid, was as effective an antigen as living virus. The incorporation of a strain of distemper virus originally thought by Horsfall, Lennette, and Rickard (1941) to exert an adjuvant effect on the influenza antigen was not found to be helpful. Bodily and Eaton (1942) added a fifth factor, which would be expected to be of significance if the results of experiments with animals are applicable to man. They compared the specificity of the antibody response following vaccination with that occurring in actual infection with virus A. The sera from vaccinated individuals were more specific in their antibody content to the strain used in the vaccine than were the sera from infected individuals to the infecting strain, although these too showed a limited degree of strain-specificity.

Notwithstanding the apparent drawbacks associated with the use of a virus vaccine subcutaneously, several trials have now been carried out which indicate that such a method of immunization is not only practicable but gives results which

indicate a measure of protection in vaccinated individuals. Our own record in connexion with such studies has hardly been brilliant. In 1937 we employed a formolized vaccine made from filtrates of the lungs of mice infected intranasally with the W.S. strain of virus A—a strain which is apparently particularly specific in antigenic constitution. Only 30 volunteers were vaccinated at an adequate time prior to the 1937 outbreak, and none of these or their controls contracted the disease. Some hundreds of other subjects were also immunized with the same vaccine, but the immunization was too late in the course of the epidemic for reliable data to be obtained. Several instances occurred of influenza A in vaccinated individuals, however, and all the virus strains recovered in the outbreak were relatively remote antigenically from W.S. We wondered if the antigenic difference between vaccinating and infecting strains was the cause of the poor result.

In 1938 we immunized 500 boys at the Naval training school at Shotley in November and December, some with a polyvalent formolized mouse-lung vaccine containing the broadly antigenic P.R.8 strain and also the W.S. strain, and some with W.S. virus vaccine only. When influenza broke out in Jan., 1939, it did not affect this particular institution. A small wave of mild influenza occurred in April, however, and we were able to recover influenza virus A from some of the cases. During the fortnight when virus A influenza was affecting the unit, 4.35% of the vaccinated and 5.4% of the controls suffered clinical attacks. The differences in incidence in the groups receiving the two vaccines were insignificant. We thought that the interval of four months between vaccination and infection meant that the effects of the vaccine had worn off by the end of this period. It was also surprising that this institution experienced its outbreak of influenza so late in the year, for other areas were affected in February and March. Again, we wondered if the number of vaccinated individuals in the community in these months was proportionately high enough to confer temporary immunity on the whole group.

Since the war we have for various reasons been unable to undertake the manufacture of enough virus vaccine for field trial. However, in 1940 a considerable quantity of the combined formolized virus A and distemper vaccine thought by Horsfall and others (1941) to be such an effective antigen was made available to the Medical Research Council for use in this country. In spite of the relatively poor antibody responses obtained on preliminary trial, we decided in 1942 to utilize the vaccine in a controlled field trial in the Army. Some 12,000 volunteers in the various Home Commands were inoculated and a similar number were set aside as uninoculated controls. The vaccination was completed by Dec., 1941, but no outbreak of influenza occurred at all in the next three months, and such tests as were carried out on sporadic cases of influenza failed to give serological evidence either of influenza A or of influenza B.

Thus we reached no conclusion as to whether this vaccine had been beneficial or not. However, Horsfall, and also Brown and his co-workers (1941), used the same type of vaccine in 1940 on some thousands of individuals, and concluded that a real reduction in the incidence of clinical influenza occurred during a subsequent virus A epidemic. The best results were that a 50% reduction occurred in certain of the vaccinated groups of individuals, but the results in other groups were not so good. Since then Francis and his co-workers have experimented with a type of vaccine produced by utilization of the phenomenon of red-cell agglutination by the virus. Virus is absorbed out from allantoic chick fluid with red cells, eluted, and subsequently resuspended in a smaller volume of fluid. These manœuvres result in a considerable separation of virus from foreign protein, and also in a concentration of virus antigen. Preliminary studies of the efficacy of the vaccine were made by exposing vaccinated individuals to an immunity test with inhalation of atomized virus A of a recently recovered strain (Francis, Salk, Pearson, and Brown, 1944). This strain was not identical serologically with the strain used for preparing the vaccine. It was found that the vaccinated individuals had a lessened febrile response to the infection, and that the effect of the vaccine was most evident two weeks after inoculation and had practically worn off four months later. The test of infection was presumably severe in that 80% of unvaccinated men exposed to a similar inhalation developed fever and 50% had temperatures over 100°.

The vaccine, which contained equal amounts of virus A and virus B, was given a large-scale field trial in 1943 during the virus A outbreak of that year. The report by members of the Commission on Influenza of the United States Army (1944), who undertook the organization of the trial, contained unequivocal evidence of the value of the vaccine under the particular conditions of the test. The percentage incidence of clinical influenza in the various groups of the 6,000 controls varied from 3.38 to 9.06, that for the groups of 6,000 vaccinated individuals from 1.15 to 5.25. The incidence of clinical attacks in the vaccinated groups was lowered on the whole to one-fourth that in the controls, and only two groups had small differences between incidence in vaccinated and that in control individuals. These figures included all cases of clinical influenza and excluded afebrile colds, follicular tonsillitis, and infectious mononucleosis. Though the result of serological analysis of the influenza cases has not yet been reported, the general prevalence of virus A during the outbreak suggests that the majority of cases belonged to influenza A. It also seemed that immunization did not begin to affect incidence—that is, to confer immunity—until at least eight days after the vaccine was given. One point is of great importance in assessing the result of this trial. Immunization was carried out in October and November with one subcutaneous dose, and the outbreaks of influenza began about the middle of November. In at least one area vaccination was begun after the epidemic was in progress, but in general an interval of two to four weeks ensued between vaccination and epidemic. It may well be, therefore, that the extraordinarily successful timing of vaccination, which was in fact a matter of chance, was an important factor in the success of the experiment. The serological response to the vaccine was actually at its peak when the outbreak of influenza occurred. It seems probable that this question of the time interval between vaccination and exposure to infection by the virus is of critical importance is deciding the effectiveness of the immunization. Not only in the case of our own experience at Shotley, but in the comprehensive trials carried out in State institutions by Muckenfuss and his co-workers in New York State (Siegel *et al.*, 1942), no difference in incidence of cases of influenza in vaccinated or control individuals was seen when the epidemic occurred six weeks or more after the vaccination. That a concentrated type of virus vaccine may still have some significant effect for as long as one year after immunization has, however, been demonstrated recently by Hirst, Rickard, and Friedewald (1944).

All these experiences with human immunization were carried out with influenza A, and much less is known concerning influenza B. Eaton and Martin (1942) showed that formolized allantoic fluid containing virus B was an effective antigen as judged by the production of neutralizing antibodies, and some of us feel that virus B is actually more highly antigenic, at any rate in animals, than virus A. Salk, Pearson, Brown, and Martin (1944) tested their formolized concentrated virus A and B vaccine by exposing vaccinated and untreated individuals to inhalation of active virus B. As in the experiment with virus A, a diminished febrile response was observed in the vaccinated individuals compared with the controls, but a higher degree of residual immunity was discernible four months after vaccination than in the case of virus A. No field trial of an influenza B vaccine has yet been reported.

In Australia the work of Burnet and his colleagues upon the production of immunity by the intranasal use of attenuated virus strains has been pursued since 1937, when it was found that prolonged cultivation of a virus A strain (Melbourne) on the chorio-allantoic membrane of the chick resulted in loss of pathogenicity for the ferret and mouse. At the same time the virus, though causing an inapparent infection of the ferret, produced an antibody response in this animal, and it thus seemed possible that the same result would be obtained in man. The work with attenuated strains both of virus A and of virus B given by nasal spray was summarized by Burnet in 1943. The essential difficulty has been to produce strains with the correct level of attenuation for man. If attenuation is carried too far, as in the case of the original Melbourne strain, the virus produces neither clinical nor serological reaction. If attenuation is not carried far enough, clinical reactions follow. Ideally attenuated virus produces good serological responses which are closely correlated with the pre-existing antibody levels to the virus and which occur in about 20 to 30% of individuals. At the same time, clinical reactions are trivial or absent in the majority, and take the form of coryza, slight headache, or malaise in the remainder. This method of immunization was tested by Bull and Burnet (1943) by determining the response to a second spraying some months after an initial inoculation. Virus B was used, and the experiment has already been referred to. Although, by the criterion of antibody response, the sprayed individuals were mostly immune three to six months later, nasal symptoms were actually more frequent after the second spraying, which suggested that such symptoms may have an allergic foundation. Repeated sprayings carried out by Mawson and Swan (1943) with mixtures of attenuated A and B strains further showed that failure to respond by antibody rise to a first inoculation was again noted after a second spraying, thus suggesting that

individual factors in resistance to infection are the cause of the failure to respond in the first place. In the experience of these workers and in that of Burnet and Foley (1940), use of a less attenuated virus strain in such individuals led to actual clinical attacks.

The effect of administration of attenuated virus strains during an actual epidemic was seen in only one unit in 1942. There, though influenza, presumably due to virus A, was actually spreading in the camps, no serious acute reaction followed such as would have suggested that spread from person to person under conditions meteorologically suitable for an epidemic would permit the attenuated virus to regain virulence. Nor, however, was much benefit conferred by the immunization, though the study was not carried out under ideal conditions. A reduction in incidence of influenza from 6.63% in the controls to 4.4% in the immunized individuals was, however, observed (Burnet, 1943). Only further experience will enable full judgment to be passed on the relative merit of this method of immunization compared with the subcutaneous method, but simplicity of production and economy of material make rapid large-scale production of the attenuated vaccine much easier than in the case of the concentrated vaccines needed for subcutaneous immunization. It is also conceivable that the time lag before immunity becomes effective is shorter with intranasal than with subcutaneous vaccines, and therefore in the presence of an outbreak the value of an intranasal vaccine would not necessarily be impaired.

Passive Immunization

I can here do no more than mention the experiments which have been made to confer resistance to influenza by passive immunization of man with serum. Earlier in this lecture I mentioned the use of immune serum intranasally in mice and ferrets, and in man successful use of atomized intranasal serum has been reported from Russia (Smorodintseff, Gulanoff, and Chalkina, 1940). Trial of this method last year by Andrewes and Glover (unpublished experiments) during the virus A outbreak gave inconclusive results because none of the groups in which the method was applied developed a sufficient number of cases of influenza in the non-serum-treated controls after the application of serum to the remainder. It was therefore impossible to draw any conclusions as to the value of the method. Possibly such a method might be of greater value during a pandemic type of influenza with high incidence of pulmonary infection by the virus.

Control of Epidemic Influenza

Rational control of any infectious disease depends on knowledge of the whole cycle of the infection, including the source of the causative agent, its mode of spread, and the factors which underlie natural resistance of the host. In the case of influenza, knowledge is still lacking on many of these points, and particularly on the source of infection and whereabouts of the virus in interepidemic times. Possible methods of control based on the mode of spread have, however, been studied, particularly since the outbreak of war. Andrewes and Glover in 1941 defined the mode of spread of contagion in the case of ferrets infected with virus A and showed that, though distant contagion by fine air-borne droplets was entirely possible, the relatively coarse droplets spread from the mouth and nose, particularly in sneezing, were also of great importance in conveying infection. Human contagion is almost certainly conveyed by true air-borne spread at times, but direct droplet infection from man to man must be important. Dust infection is also possible, as shown by the experiments of Edward (1941) on the resistance of influenza virus to slow drying at room temperatures. The great developments which have taken place in recent years in methods of sterilization of the air were reviewed by Andrewes in 1940 and Stuart Mudd more recently (1944). Air-borne particles of influenza virus have been shown to be capable of destruction by such methods as ultra-violet irradiation (Wells and Brown, 1936), or by germicidal mists or vapours such as hypochlorous acid gas (Edward and Lidwell, 1943) or propylene glycol (Henle and Zellat, 1941). Stokes and Henle (1942) have used propylene glycol vapour in a ward, and have demonstrated that atomized influenza virus released into the air is thereby destroyed.

All these methods may play a definite part in the reduction of air-borne infection in crowded messrooms, air-raid shelters, and places of entertainment. They would inevitably be less successful against the direct spread of coarse droplets over short distances, and, though the wearing of masks would provide ideal barriers against such droplets, experience has shown that people will not readily tolerate such measures. The limitations of physical and chemical methods of introducing barriers to the spread of virus during outbreaks of influenza are therefore considerable. Not much more than a reduction of incidence in particular groups where overcrowding would produce an abnormally high rate can be hoped for so far as the uncomplicated virus infection is concerned. There seems more hope that complications may be reduced in incidence, and in pandemic influenza the value of methods of aerial hygiene would be most definite. I do not propose to elaborate this type of work further, as I have not myself taken part in it. I would, however, point out the fact that, even without special apparatus or knowledge, simple measures of hygiene such as improvement in window ventilation, spacing out of beds, and encouragement of a hygienic attitude towards coughing and sneezing may do much to lower the incidence of infection in disciplined communities such as Army units.

When we turn to survey the problem of control of influenza in general it is obvious that the usefulness of all prophylactic methods is dependent on the particular variety of influenza which it is desired to control. In regard to the type of influenza experienced in recent years, there would be little room for methods which failed to reduce actual incidence though they affected severity or incidence of secondary complication. In the face of an outbreak of influenza of the 1918 type, however, any method which modified the course of infection, even if it failed to prevent it completely, would be of use. Naturally, also, there is, in wartime, increased scope for control measures against influenza in order to effect a reduction in the loss of labour to industry or of time to duty from minor as well as major sickness, and measures which fall short of perfection would be relatively more acceptable now than in times of peace. We have seen the promise held out by methods of artificial immunization in limiting the incidence of infection during an outbreak, and the problem would seem essentially to be the application of the method. In such a periodic disease as influenza we are enormously handicapped by lack of knowledge as to when to expect epidemics. The fact that the methods available for artificial immunization are probably effective for only short periods after inoculation adds further difficulty. It will clearly be useless to immunize unless there is a reasonable probability of an outbreak within the next few weeks or unless the outbreak has already begun in neighbouring areas. Use of a vaccine after an epidemic has begun may not be actually harmful, but, in view of the delay before subcutaneous vaccine exerts an effect, only intranasal virus would then have much chance of success. If we are lucky enough to experience indicator outbreaks during the months preceding an epidemic, as occurred in 1943, then we may be able to apply immunization with benefit, but unfortunately we do not yet know whether such experience is exceptional or not. Should we desist from attempts at immunization because of the argument that we owe our present freedom from a recurrence of pandemic influenza of the worst variety to the regular recurrences of the type of mild influenza which we have been considering? My own view coincides with that of Stuart Mudd (1944), who believes that the dissemination of agents of respiratory disease should be attacked whole-heartedly by all possible methods. On the other hand, there is clearly much room for improvement both in how best to apply vaccines and in their actual composition. An example of possible future developments lies in the recent discovery of Friedewald (1944) that the addition of certain substances—of which a mixture of liquid paraffin, killed human tubercle bacilli, and a lanolin-like absorption base known as falba was the most effective—has an amazing adjuvant effect on the antigenic power of influenza virus, and increases the size and duration of the antibody response to virus given subcutaneously. The application of the methods of aerial sanitation in addition to immunization will certainly be necessary if ever we are faced by a recurrence of pandemic

influenza of the 1918 type; and there is the undoubted possibility, as already mentioned, that the causative organism of such influenza may be entirely different in type or in antigenicity from the viruses so far studied. Faced by a virus of entirely novel antigenic type, it is unlikely that any of our present vaccines would have any beneficial effect at all, and we should probably have to spend our time studying the new agent in the laboratory during the period when it was wreaking its vengeance on ourselves and our fellows. General methods of hygiene as well as the methods of aerial disinfection would be our only prophylactic weapons. The use of quarantine for island communities, as in Australia in 1918, may only postpone the fatal day when the pandemic virus begins to spread among the population; but such postponement, in addition to allowing time for the development of specific methods of attack in the laboratory, might mean that the virus then would be less virulent than if it reached the area at the height of its passage through the population elsewhere.

Conclusion

To summarize: the development of knowledge concerning the mechanism of immunity and of resistance to influenza virus infection has been traced in experimental animals and in man. In animals and in man immunity is found to be a complex process, in which the production of antibodies plays only a part. Other processes, though less well outlined, belong to the innate resistance of the mucosa of the respiratory tract, which appears to possess methods of defence by virtue of the nasal secretion in addition to more definitely cellular activities. Possible ways of producing immunity in animals and in man have been described, and the general problem of control of influenza, particularly by the use of the methods of aerial sterilization, have been mentioned.

No speaker on the subject of influenza has any right to conclude a review such as I have attempted without once again emphasizing the fact that we are so fundamentally ignorant of many of the vital links in the chain of the natural infection that the need for more research on this aspect is still pressing, and must occupy as much of our time as methods of application of knowledge so far gained, or even more.

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The Empire Rheumatism Council was established eight years ago to organize research throughout the British Empire into the causes and means of treatment of rheumatic disease. The annual report for 1944 is signed by the chairman, Lord Horder, who welcomes an intimation from St. James's Palace that the Duke of Gloucester wishes to continue as president during his term as Governor-General of Australia, and that absence over-seas will in no way diminish his Royal Highness's interest in the Council's work. A committee on postgraduate education has been set up, with Sir Adolphe Abrahams as chairman. The report confirms a recent announcement in these columns that the tests so far made with a Russian serum have not justified recommendation of its use; but in view of the high reputation of Soviet medical research the Council proposes, when war conditions permit, to invite the Russian scientist responsible for the treatment to visit this country, or, alternatively, to send a research worker to Moscow to make further investigations. The Council looks forward to great progress in the field of clinical research on rheumatic disease when the establishment of a national chain of treatment centres will enable comprehensive tests under full control conditions to be made for evaluating present means and proposing new means of treatment. The *Annals of the Rheumatic Diseases*, by agreement between the Empire Rheumatism Council and the Council of the British Medical Association, is now published by the B.M.A. at Tavistock Square.

DUODENAL ILEUS IN THE NEWBORN

BY

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Duodenal obstruction in the newborn may be associated with a complete atresia or with stenosis caused either by narrowing of the bowel wall or by partial obliteration of the lumen by a membrane. It is, however, with duodenal ileus due primarily to external pressure that we are dealing in this paper.

In 1930, and later, Miller and Gage (1930, 1932, 1935a, 1935b) published a series of papers under the headings "Gastromegaly and Chronic Duodenal Ileus in Childhood" and "Chronic Duodenal Ileus in Infancy and Childhood," describing cases of obstruction to the second and third parts of the duodenum. They considered that there were two separate mechanical factors at work in producing ileus: first, a congenital anatomical factor, where a band of mesentery, usually associated with the superior mesenteric artery, was stretched across in front of the duodenum, causing some degree of compression; and, secondly, the vicious circle likely to be set up by this. They showed how the proximal duodenum tended to become distended and how this, in turn, caused ptosis and kinking over the band, so making the ileus more severe. They stressed the great importance of the latter factor in the causation of symptoms, and showed that if it could be overcome by medical treatment the baby would thrive even though the anatomical factor remained.

Ladd and Gross (1941) gave an excellent description of a further group of cases together with a bibliography. In this group, volvulus of the midgut was superimposed upon a high intestinal obstruction caused by external pressure on the duodenum. They gave a clear description of the embryological basis for the condition. Between the 6th and the 10th week of foetal life the intestinal tract grows more rapidly than the abdominal cavity, and the midgut passes out into the base of the umbilical cord. When, later, the relative rate of growth changes once more, the gut returns to the abdomen and, in the process, it rotates. It follows that the caecum at one stage comes to lie high up on the left and only later passes across to the right upper abdomen and finally to its adult position. When the process is complete the caecum has its peritoneal attachment in the right iliac fossa, while the small intestine is anchored by a diagonal attachment on the posterior abdominal wall extending from the duodenojejunal junction above to the caecum below. The normal process may become arrested at any stage. If the caecum has not reached its final position it may lie across the duodenum, high up and to the right, so that its peritoneal attachment may cause duodenal obstruction. Associated with this, the fixation of the small intestine is likely to be abnormal and volvulus of the mobile midgut may occur.

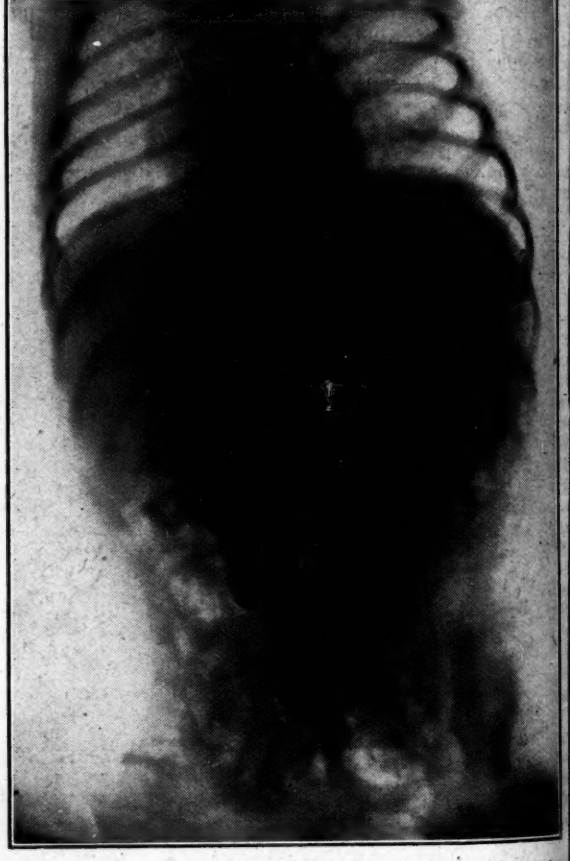
Symptoms and Signs

Vomiting is usually the predominant symptom in any form of duodenal obstruction; it is generally forcible, occurring immediately after each feed, and the vomit is often bile-stained. When present this last sign is of great value in diagnosis. Miller and Gage have noted the fact that anorexia is usually pronounced and that if the baby is not forced to take more than it wants its intake is so small that duodenal distension and the onset of vomiting may be delayed. Constipation may be very severe owing to starvation, but the stools, when passed, show no evidence of digestive upset. In the first days of life, when the differential diagnosis from duodenal atresia may be difficult, the identification of cornified epithelium in the meconium may be a valuable finding, proving that obstruction to ingested material has not been complete. Wasting and dehydration vary in degree according to the severity of the case. Distension is limited to the upper abdomen in simple cases; when it becomes more severe the complication of volvulus is to be feared. Visible peristalsis of the stomach may be seen, though not as marked as in pyloric stenosis; duodenal peristalsis, passing downwards on the right, has also been noted. On palpation of the abdomen, failure to find the characteristic firm pyloric tumour is an important point in the differential diagnosis between duodenal ileus and pyloric stenosis, though it is possible to mistake the duodenum, if distended and filled with curd, for the pylorus. The general examination of the baby includes inspection of the limbs and fontanelle in search for any evidence of a cerebral cause for vomiting, and also the elimination of any possibility of parenteral infection in the ears, urine, chest, and elsewhere. A straight *x*-ray film may be sufficient to show fluid levels in both stomach and duodenum, together with gross distension of the latter. Ladd and Gross give a warning against barium meals in these cases as they believe that the barium may become inspissated. With care there should be very little danger, and the results may be of great value in diagnosis.

Case I

First seen Dec. 31, 1940, at the age of 3 weeks. A first child born 2 weeks before term after a normal labour, the baby had appeared healthy at birth and had weighed 7 lb. 12 oz. Vomiting started "directly the milk came in," usually occurring immediately each feed had been taken, though it might be delayed for an hour. The vomit was greenish yellow in colour, and "sometimes he seemed to pump up more than he had taken." Constipation was severe, the baby had had only 4 stools during the 3 weeks of life, and had followed soap enemata. There was nothing relevant in the family history.

On examination the baby was very thin, weighing 1 lb. 4½ oz. less than its birth weight. In spite of this the general condition was reasonably good, and the infant looked starved rather than ill; there was no gross dehydration. Seen at a feed, there was no visible peristalsis, though slight distension was observed in the upper abdomen; no tumour was palpable and the hernial orifices were normal. There was no evidence of disease elsewhere. In view of the history of persistent forcible vomiting of bile-stained fluid associated with severe constipation a partial obstruction could be



Barium-meal examination of Case I. Radiograph showing dilatation of the first and second parts of the duodenum.

visualized, situated distal to the entrance of the common bile duct but at a point high up in the intestine, since there was no general distension. A tentative diagnosis was made of duodenal ileus due to compression of the third part by mesentery.

Treatment.—The baby was admitted to hospital. After gastric lavage a barium meal (see Fig.) was given; the report read: "Oesophagus normal. Stomach normal in situation. Emptying occurred readily. The first and second parts of the duodenum are grossly dilated. There is vigorous peristalsis in this area. The site of the obstruction is at the junction of the descending and ascending portions. The obstruction is only partial and may settle down." The aim of medical treatment was to empty the stomach and duodenum completely twice a day so as to enable them to regain their tone and prevent the vicious circle produced by distension and kinking. With the same end in view, feeds were small and frequent. Gastric lavage was continued twice daily for the first week; the intervals were then gradually increased till a clear result was obtained after four days without treatment. Feeds at first were given at 2-hourly intervals, with 10 feeds in the 24 hours; the intervals were then increased to 2½ hours on the 3rd day and 3 hours on the 9th day. By the 16th day the infant was able to take 3 oz. every 3 hours. On this treatment vomiting ceased almost at once and there was only very occasional sickness after the first 24 hours. The bowels moved normally on the 2nd day and caused no further trouble. There was an improvement in weight, and the baby gained steadily. He was discharged after 24 days in hospital, having gained 25 oz. and being free of all symptoms.

Barium Meal, Jan. 15, 1941.—"Repeat examination. Stomach emptied quite well. There was no hold-up in the duodenum. Stenosis can still be recognized, however."

The child was seen again on Nov. 7, 1944, at the age of 3 years and 11 months. He was well developed and in excellent health. He had been free from symptoms since leaving hospital. A barium meal showed no abnormality of the stomach or duodenum.

Case II

This patient was first seen on Dec. 10 at the age of 15 days. He was a first child, born at full term after a rapid normal labour: birth weight 7 lb. 10 oz. He appeared normal at birth. Vomiting began directly feeds were taken, and persisted for 3 days, occurring after practically every feed. The vomiting had then ceased suddenly and completely, and for the 5 subsequent days the baby took well from the breast and gained weight. Sickness returned on the 8th day and was very severe; it was frequently projectile and the fluid was usually bile-stained. The family doctor had seen peristalsis and palpated a tumour. There had been no bowel action for 4 days. Since the return of the sickness the breast milk had been expressed and given at half strength. The family history showed nothing relevant.

On examination the baby's weight was 6 lb. 9½ oz. He was thin, but, considering the history, the general condition was fairly good and dehydration was only of moderate degree. Seen at a feed, there was some distension in the upper abdomen, but no peristalsis was visible and no tumour could be palpated. A projectile bile-stained vomit occurred immediately after the feed. Except for slight umbilical discharge nothing abnormal was found elsewhere, and a normal stool was passed. Consideration of the history and physical signs suggested that we were dealing with a case similar to the one already described, and the same provisional diagnosis was made. The obvious difference between the two cases lay in the fact that in Case II there had been one complete spontaneous remission between the 3rd and 8th days of life. Mother and baby were admitted to hospital. In view of the fact that the family doctor had seen peristalsis and palpated a tumour, eumydrine was given for 36 hours, although it was felt that bile-stained vomit should rule out the possibility of pyloric stenosis. The drug had no influence on the vomiting, and was discontinued. In spite of treatment on the same lines as Case I there was no improvement. The baby was therefore put into the Trendelenburg position and the duodenum aspirated with a Ryle's tube; continuous duodenal drainage was kept up for some hours and subsequently repeated at frequent intervals. Additional fluid was given by the subcutaneous route and by continuous rectal drip; half-strength saline, followed by tap-water and glucose, was absorbed extremely well from the rectum. Since there was no fault in digestion and the baby took well, the caloric value of the feed was increased by the addition of 1 dr. of half-cream dried milk powder to each 4 oz. of breast milk. After a day of this treatment the baby for more than 24 hours did not vomit and the bowels opened normally. Unfortunately the sickness returned and persisted with far greater intensity in spite of continued treatment, so that the infant went downhill rapidly and died 2½ days later, 8 days after admission to hospital.

When the vomiting returned, after the short interval of freedom, the question arose whether laparotomy was advisable. Various factors had to be considered. The infant was in poor condition; there had been two remissions, and a third might possibly occur. Looking back, in view of the post-mortem findings (see below) it is just possible that surgery might have been successful even two days before death. We can only make a conjecture as to the sequence of events inside the abdomen. It seems probable that the partial obstruction had been caused in the first place by pressure on the duodenum, either from malposition of the caecum or from the primitive mesentery around the superior mesenteric artery. Then, with the onset of continuous sickness 2½ days before death, a volvulus of the midgut had been superimposed. The volvulus might easily have been relieved surgically, and Ladd and Gross describe a simple operative procedure by which they free the caecum from its attachment high up on the right and allow it to fall across to the left of the abdomen, in which position it can no longer obstruct the duodenum.

Post-mortem Report.—The relevant extract from the report reads as follows: "The body of a small, rather wasted male infant. The head appeared rather large, the fontanelles were a little depressed. The skin was loose. The upper part of the abdomen was somewhat full, though the lower part was insunken. . . . *Abdomen:*—Peritoneal cavity: The stomach was rather large and distended. The duodenum was grossly distended, being almost as large as the stomach. The distension stopped abruptly at about the mid-point of the third part of the duodenum. At this point the duodenum was involved in a volvulus which had occurred at the root of a primitive mesentery around the superior mesenteric artery. The volvulus was left-handed. It was not so tight as to have interfered with the blood supply of the small gut, though tight enough to have prevented the passage of intestinal contents beyond the point of volvulus. The descending and transverse colons were in the normal situation, but the caecum lay on the anterior aspect of the immensely distended second part of the duodenum. The long appendix passed medially over the distended third part of the duodenum. The absence of the caecum from the right iliac fossa, and the drawing up of the small intestine by the volvulus, accounted for the fallen appearance of the lower abdomen. There were no further abnormalities in the abdominal cavity." The body was otherwise natural except for a very few pericardial haemorrhages and a fairly severe tear of the upper leaf of the tentorium on the left, which had healed over, though there was some extravasation of blood into the substance of the tentorium.

Summary

Two cases of duodenal obstruction in the newborn are described. They illustrate two types of case. The first resembled those described by Miller and Gage and responded rapidly to medical treatment. The second probably began in a somewhat similar way, but volvulus was superimposed and caused the infant's death.

I am indebted to Dr. Robb-Smith, Director of Pathology, Radcliffe Infirmary, Oxford, for the post-mortem report, and to Dr. Kemp, radiologist to the hospital, for the *x*-ray reports and the print.

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BURNS AND THEIR TREATMENT AMONG E.M.S. HOSPITAL IN-PATIENTS

BY

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Examination of the records of the E.M.S. Statistical Branch at Norcross shows that of the total injuries for which Service patients were admitted to the E.M.S. hospitals, burns caused among men about 3% in 1942 and 4% in 1943, and among women about 10% in each year (Stocks and Brooke, 1944). At Norcross every fifth record of admission for in-patient treatment is selected, and the primary, secondary, and complicating causes of admission are coded by means of the Medical Research Council's Classification of Diseases and Injuries. In the code numbering for burns the third digit indicates the agent causing the disability and the fourth digit the part of the body affected. A random sample of 400 of the cases admitted on account of burns during 1943 and the first half of 1944 has been examined in detail, and an analysis of the distribution according to age and site is given in Table I.

Six males and one female died—a proportion of 1.75%. Five deaths of men were due to extensive burns caused by aeroplane crashes. In each case the patient was very shocked

TABLE I.—*Distribution of Burns according to Age and Site*

M.R.C. Code No.	Site of Burns	Males						Females					
		15–	25–	35–	45 up	Total	%	15–	25–	35–	45 up	Total	%
93–0	Face, head, or neck	24	20	9	0	53	14·9	4	2	1	0	7	15·5
93–1	Trunk	3	6	1	0	10	2·8	0	0	0	0	0	—
93–2	Upper limb or limbs	10	12	2	0	24	6·8	2	5	1	0	8	17·8
93–3	Hand or hands	27	32	10	0	69	19·4	3	1	0	0	4	8·9
93–4	Lower limb or limbs	19	33	13	3	68	19·2	12	4	0	1	17	37·8
93–5	Face, head, or neck, and also trunk and limbs	2	9	0	0	11	3·1	1	0	0	0	1	2·2
93–6	Face, head, or neck and also limbs	36	28	6	0	70	19·7	3	0	0	0	3	6·7
93–7	Trunk and limbs	10	5	1	0	16	4·5	1	0	0	0	1	2·2
93–8	Other or unqualified areas	14	11	8	1	34	9·6	2	2	0	0	4	8·9
	Total	145	156	50	4	355	100	28	14	2	1	45	100
	Percentage	40·9	43·9	14·1	1·1		100	62·2	31·1	4·5	2·2		100

and, despite blood or plasma transfusions and such other treatment as it was possible to give, four died on the day of admission to hospital, and the fifth four days later. The death of a woman was due to toxaemia. Five men and one woman were discharged from the Services as a result of their injuries, after periods of treatment ranging from 162 to 378 days.

TABLE II.—*Distribution of Burns according to Agent*

M.R.C. Code No.	Agent	Males		Females	
		Frequency	%	Frequency	%
930–	Fire and hot objects	164	46·2	6	13·3
931–	Hot liquids and vapours	80	22·5	25	55·6
932–	Corrosive liquids	14	3·9	3	6·7
933–	Radiations	1	0·3	—	—
934–	Electric currents	2	0·6	1	2·2
935–	Other or unqualified	93	26·2	10	22·2
936–	Sunburn	1	0·3	—	—
	Total	355	100·0	45	100·0

The distribution of burns according to agent is shown in Table II. Of the 170 burns caused by fire and hot objects, many of which were avoidable accidents, 42.9% were due to burning petrol, 24.7% to flames from fires, blow-lamps, cookers, etc., 13.5% to incendiary bombs and other instruments of war, and 18.9% to miscellaneous agents. Phosphorus caused 10.75% of all burns (included in No. 935–).

Tables III and IV show the distribution and the median number of days of treatment of burns by site and degree. The period of in-patient treatment given for a burn depends not only on its severity and the site and size of the affected area, but also on whether adequate after-care can be provided at the man's unit, in which case he can be discharged before the injury is completely healed. Since this applies chiefly to cases of long duration, the median number of days' treatment for different degrees and sites provides a better measure for comparison than would a complete tabulation of periods of hospitalization or an arithmetical mean of these periods.

The median is naturally high for numbers 93–5 and 93–7, which are for multiple sites. The high median for 93–4, lower limb or limbs, is partly accounted for by there being 8 third-degree burns in this group as compared with 3 at most in any other.

TABLE III.—*Distribution of Burns according to Site and Degree*

M.R.C. Code No.	Site	Degree									
		Males					Females				
		1st	2nd	3rd	Not Stated	All Types	1st	2nd	3rd	Not Stated	All Types
93–0	Face, head, or neck	13	15	3	22	53	3	3	0	1	7
93–1	Trunk	1	3	1	5	10	0	0	0	0	0
93–2	Upper limb or limbs	0	10	3	11	24	0	5	0	3	8
93–3	Hand or hands	5	34	2	28	69	1	2	0	1	4
93–4	Lower limb or limbs	1	31	8	28	68	4	4	0	9	17
93–5	Face, head, or neck, and also trunk and limbs	1	4	2	4	11	0	0	0	1	1
93–6	Face, head, or neck, and also limbs	10	31	2	27	70	1	0	0	2	3
93–7	Trunk and limbs	1	7	0	8	16	0	1	0	0	1
93–8	Other or unqualified areas	2	17	3	12	34	1	2	0	1	4
	Total	34	152	24	145	355	10	17	0	18	45
	Percentage	9·6	42·8	6·8	40·8	100	22·2	37·8	0	40·0	100

TABLE IV.—*Median Period of Treatment, according to Site and Degree (including Period of Treatment at Unit before Admission)*

M.R.C. Code No.	Site	Median Number of Days' Treatment							
		Males				Females			
		1st Deg.	2nd Deg.	3rd Deg.	All Types*	1st Deg.	2nd Deg.	3rd Deg.	All Types*
93–0	Face, head, or neck	13	11	20	15	5	7	—	7
93–1	Trunk	—	11	—	14	—	—	—	—
93–2	Upper limb or limbs	—	17	21	18	—	19	—	19
93–3	Hand or limbs	16	14	—	16	—	—	—	17
93–4	Lower limb or limbs	—	37	120	45	15	35	—	26
93–5	Face, head, or neck, and also trunk and limbs	—	37	—	53	—	—	—	—
93–6	Face, head, or neck, and also limbs	18	20	30	19	—	—	—	21
93–7	Trunk and limbs	—	37	—	63	—	—	—	—
93–8	Other or unqualified areas	—	28	—	31	—	41	—	39

* Including burns for which the degree was not stated.

Summary

A statistical analysis is presented of a random sample of 40 in-patients from the Services admitted to all E.M.S. hospitals during 1943 and the first half of 1944 on account of burns. Distribution according to sex and age of patient, site and degree of burn, and duration of treatment are given; and the method of sampling was such that these may be regarded as representing the average experience in E.M.S. hospitals during the period.

I am indebted to Sir Francis Fraser, Director-General of E.M.S., Sir Claude Frankau, Director of E.M.S. in London and the Home Counties, and Dr. P. Stocks, General Register Office, for their help and suggestions.

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R. F. Norris, R. A. Kern, H. P. Schenck, and L. E. Silcox (*U.S. nav. med. Bull.*, 1944, **42**, 518), who report an outbreak of 18 cases of diphtheria in a U.S. naval hospital ship in the Solomon and neighbouring islands, state that the efficiency of antitoxin suggests that there is no fundamental difference between the strain of *C. diphtheriae* in the Tropics and those in the U.S.A. Since diphtheria in the Tropics is a comparatively mild disease, it often goes unrecognized and may be followed by fatal peripheral paralysis.

TREATMENT OF THE PATIENT WITH BURNS, WITH REFERENCE TO THE PROFLAVINE POWDER TECHNIQUE

BY

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The trend of modern surgical thinking is to focus attention upon a stated lesion rather than to take into conception a view of the patient as a whole. In certain diseases the actual lesion is the outward sign of a complex interplay of pathophysiological processes affecting the whole organism. The corollary is also true as applied to the effects of injury. The local damaged area calls the same general processes into action, and it is important to recognize and understand the reactions of the body to injury. It has become commonplace to discuss treatment under two headings—general and local—but too often inadequate attention is given to the former. Since the measures instituted in the general treatment often exert a local action, and vice versa, it appears advisable to modify this classification and to consider the patient as a whole. The patient with a major burn must be treated from this point of view.

Since the outbreak of the present war the subject of burns has received considerable attention and our knowledge has consequently been enriched. The division of the local lesion into three degrees instead of the classical six of Dupuytren is helpful, but it is pointed out that several days usually elapse before it is possible to classify a burn, and all three degrees may be represented. The psychological aspect requires attention, especially with major burns in exposed parts of the body—reassurance and encouragement must be given as regards scarring, with disfigurement and dysfunction. In burns of the face an early inquiry with respect to these matters is usually made by the patient. For the relief of pain morphine must be given in adequate amounts, and if a quick result is desired it should be administered by the intravenous route. Interesting experiments have been carried out on the effects of nembutal, and it is reported to reduce the fluid loss of the burned surface. If these results are confirmed and applied clinically this drug may be used also as a soporific with a double advantage.

Plasma Loss

This is rapid at onset, and may be severe in amount. Further, the loss of plasma is a continuous process extending over a long period of time in the injured area. As a result, hypoproteinaemia develops. In the pathogenesis of this condition more than one mechanism is operative. There is the loss of plasma at the site of injury, and in addition the output of nitrogen in the urine is increased. The patient is unable to ingest an adequate protein diet during the initial period following his injury.

Later there may be damage to the liver as the result of toxic absorption, with consequent impairment of function in the synthesis of plasma albumin. Acute hypoproteinaemia may develop a few hours after a severe burn, and both its presence and its degree must be rectified and corrected. Chemical analysis of the blood should be carried out and the plasma albumin fraction measured. In addition, the haemoglobin percentage must be determined, together with an enumeration of the red blood cells. To rectify this condition plasma transfusion is required as early as possible and in adequate amount. In severe cases a minimum of 1,000 c.cm. is given at once, and quickly in rate. Further quantities may be necessary over a period of time, and the clinical condition of the patient is the simplest guide. Fluid-balance charts must be instituted and the output of urine watched carefully. When the patient is able to ingest it, he should be put on a high-protein diet containing a large proportion of essential amino-acids. For an adult of average size 150 g. of proteins per day can be given, the best foods being milk, lean meats, and eggs. Amino-acids may be given orally if there are digestive disturbances, but this is an expensive method. In an excellent review of this subject Elman and Lischer (1943) call attention to the value of amigen, an enzymic digest of casein and pork pancreas containing amino-acids and a small quantity of polypeptides. Amigen can be administered orally and intravenously; as much as 300 g. has been given in 24 hours by the latter route. A high protein intake is necessary to safeguard the live cells from the effects of toxic absorption.

Sulphonamide Therapy

It is not our practice to give sulphonamide drugs orally as a routine. In cases of severe toxic absorption and liver insufficiency they may be harmful. Each patient must be carefully considered from this angle and the general condition assessed. Oral chemotherapy is beneficial in cases of haemolytic streptococcal infection with marked pyrexia. An adequate fluid intake is necessary and the response of the patient should be carefully noted. We have ceased to employ these drugs locally in the injured area.

After a period of three or four days secondary anaemia frequently develops, and becomes marked unless measures are taken to combat it. Iron therapy, using massive doses, is instituted. In severe burns one or more blood transfusions may be required during the second and third weeks, and it is our practice to transfuse when the haemoglobin falls below 70%. Hypovitaminosis is corrected by the daily administration of vitamins B and C. Careful attention to the cardiac and respiratory systems is necessary, especially in elderly patients, and cardiac failure or pulmonary infection is treated along routine lines. In the case of septic burns constant scrutiny of the condition of the heart, liver, and kidneys is essential.

In countries where malaria is endemic this infection may be a complicating factor in cases of burns. We have shown elsewhere that trauma may precipitate an attack of malaria in a patient whose disease is quiescent. Thus in patients who are pyrexial in malarious areas it is a wise precaution to examine the blood for malaria parasites on several occasions.

Treatment of the Wound

Wound treatment is carried out under strictly aseptic conditions in the operating theatre, usually without general anaesthesia; morphine should be administered subcutaneously half an hour before the operation, and in severe cases this can be given intravenously with good effect. The toilet of the wound is careful and conservative. Contaminants are mopped away with a solution of normal saline, and pieces of dead tissue are lifted off. Normal skin surrounding the wound is carefully cleansed with spirit. Blisters are evacuated carefully by pricking with a sterile needle. Dry proflavine powder is lightly smeared over the wound, the whole lesion being thinly coated. The wound area is covered with one layer of wide-meshed gauze impregnated with vaseline and, over this, two layers of wide-meshed gauze with a liberal supply of cotton-wool. The dressing is bandaged firmly to form a pressure-dressing with either plaster-of-Paris or calico bandages, and this initial dressing is not removed for a minimum period of five days. After the first re-dressing the time-interval between dressings is increased from 10 to 14 days. Proflavine powder is dusted on the wound at each re-dressing. The wounds in burns of third degree should be skin-grafted as soon as they are in a satisfactory state.

Use of Plaster-of-Paris

We have with advantage used plaster coverings for the dressing in certain parts of the body. Attention is called to the value of the "plaster glove" for the treatment of burns of the hand. The toilet is carried out as described, each finger being covered separately with vaselined gauze and dry gauze. The following technique is employed for the application of the "plaster glove."

The patient is instructed to place the hand in the position of rest, the fingers being partially flexed at the interphalangeal and metacarpo-phalangeal joints, with the tips of the index finger and thumb in opposition. The wrist-joint is held in partial dorsiflexion. A rolled pad of cotton-wool is placed in the palm of the hand as a support for the fingers, and the hand and forearm are covered with a liberal supply of that material. The hand, wrist, and forearm are then encased completely in the plaster glove, which extends as

high as a point two inches below the elbow-joint. The limb is elevated for several days in order to minimize tissue oedema. Active exercises are instituted for the fingers after 48 hours, together with active exercises at the elbow- and shoulder-joints.

In the case of burns of the foot a similar technique is employed. The glove is left in position for a period of two to three weeks. Other regions of the body have been treated by the proflavine-plaster technique, including the leg, thigh, forearm, arm, shoulder, chest wall, and abdominal wall. In the case of large joints such as the knee and elbow, bandages are applied, with plaster above and below, in order that active exercises may be carried out. There are several advantages in the plaster technique. The dressing is comfortable and is held firmly in position. If evacuation of the patient is necessary, travelling in plaster is comfortable. In tropical and subtropical countries, where flies are numerous, the plaster forms a barrier against maggot infestation.

In order to illustrate the results obtained reference is made to the following typical cases among those we have treated by the powder. It is our practice to investigate the bacterial flora present in the wound from its inception until healing occurs. On account of the necessity for evacuation it was not possible to hold every patient until healing was established. Nevertheless we have investigated sufficient cases treated by this method to be very impressed with the end-results.

Illustrative Cases

Case 1.—Trooper aged 30. Admitted with major burns—second and third degrees—involving face, neck, forearms, hands, right chest wall, anterior abdominal wall lower half, penis, scrotum, right buttock, and both thighs. Treated with proflavine powder as described. Plasma transfusion 1,350 c.cm. Bacteriology of burns showed coliform organisms. Four days after admission, plasma transfusion 1,350 c.cm. Seven days later re-dressed. Coliform organisms present. He was re-dressed at intervals, and bacteriological examinations showed *B. proteus, Staph. aureus,* and coliform organisms. Thirty-six days after the first treatment the wounds were clean, sloughs had separated, and healthy granulation tissue had formed. All areas not healed were skin-grafted, using split-thickness grafts. There was a good "take," and in 69 days the patient was evacuated in good general condition, walking well, and all wounds had healed save a small patch on the right thigh which was in process of healing.

Case 2.—Fireman aged 38. Admitted with major burns—second and third degrees—involving both lower extremities, buttocks, penis, and lower part of the back. The patient had been treated at another hospital, the injury having occurred 18 days before we saw him. He had received sulphathiazole orally, 45 g., and sulphanilamide powder locally. His general condition was very poor and secondary anaemia was present—Hb 68%. Two pints of blood were transfused and routine proflavine treatment given for the burns, which were very infected. A second blood transfusion, one pint, was given 12 days later and again on the 47th day. Dressings were changed at intervals, and bacteriological investigations showed *B. proteus, Staph. aureus,* coliforms, and diphtheroids. Patient was evacuated 67 days after admission in good general condition, walking well, and with wounds healed.

Comment

It is of interest to compare Cases 1 and 2, as these burns were of comparable severity. In Case 1, treated with proflavine powder, the general condition did not show the marked toxicity of Case 2, and no blood transfusions were required as in the latter. The lengths of stay in hospital before healing was achieved were 69 and 67 days respectively. The haemolytic streptococcus was absent in all cases, and we believe that such infection can be prevented by the use of this method. Bacteria met with in our cases were *Staph. aureus* and *albus, B. proteus,* coliforms, diphtheroids, and *B. pyocyaneus.* In the past it has been stated that the acridine compounds retard the healing process in a wound. This has not been our experience using powdered proflavine in burns and also in other types of wounds. On the contrary, healing is usually rapid and there is a noticeable absence of scarring, the resulting skin being supple and of excellent quality. The hands we have treated are functioning normally and no contractions have developed. It is recognized that a burn of the hand may be of such severity that a deformity will result no matter what treatment is given. There has been no instance of a deleterious general effect from absorption of proflavine at the wound surface.

Summary

In the treatment of burns the patient as a whole must be careful considered, and the salient features in his management are he discussed. Powdered proflavine has been used in the treatment the wound and the results achieved are described. This chemic substance is of proved value, and we employ it as a routine. Atte tion is called to the use of plaster-of-Paris as a covering for t dressings, and in particular to the "plaster glove" in burns of t hand. Proflavine powder does not retard the process of healin and the resulting healed area showed a remarkable freedom fro scarring, the skin being supple and of excellent quality.

I am indebted to Major T. Day, R.A.M.C., for carrying o bacteriological examinations on a large series of patients. C W. A. Y. Knight, A.M.S., commanding the hospital, has kind allowed me to publish the case histories.

Reference

Elman, R., and Lischer, C. E. (1943). *Surg. Gynec. Obstet.*, **76**, Int. Abst. Sur 503.

Medical Memoranda

Enucleation of Six Ovarian Dermoid Cysts fro one Woman, with Conservation of the Ovaries

The following case record illustrates the scope of conservati surgery on the ovaries.

Case History

Miss J., aged 21 (No. 24703). During a routine examinatio a swelling was found in this girl's abdomen. At the West Londo Hospital a provisional diagnosis of ovarian cyst was made, and h name was placed on their waiting list. As a result of the air ra in London in the early months of 1944 she came to Oxford a was admitted to the Radcliffe Infirmary. On the previous diagno with which I had no reason to disagree, the abdomen was open The operative details are as follows:

Left lower paramedian incision. A bluish cystic swelling aris from the left ovary was immediately apparent; it was about 9 long, and had the appearance of a multilocular ovarian cyst w an extension running up towards the left. The uterus was norm in size and position. The right ovary was about 5 in. long, a clearly contained two separate cysts, one at each pole. Each c in the right ovary was a little smaller than a golf ball, and w yellowish in colour, as if filled with sebaceous material such as commonly present in dermoid cysts.

These two cysts in the right ovary were both enucleated ea and bloodlessly, and the ovary was repaired. Because of the fi ings in the right ovary the loculated swelling of the left ovary w re-examined. Though each locule was obviously filled with wat fluid, there were in addition a few fat globules to be seen throu the capsule. On the supposition that the left-sided cyst was also dermoid, enucleation was proceeded with. Surprisingly, the c turned out to be not one but four quite separate ovarian dermoi Three were enucleated without difficulty, though one was accidenta punctured; the fourth was removed along with a piece of thinn out ovary. The ovary was repaired and the abdomen closed.

Convalescence was uninterrupted. Before operation the pati menstruated every two months; subsequently she reported her peri as "regular every month."

All six cysts contained hair. The two on the right side w largely filled with sebaceous material; the four on the left with watery fluid. Histological examination confirmed the clini diagnosis of benign cystic ovarian dermoids; a great variety of ti elements were identified.

COMMENT

Dermoid cysts of the ovaries are not infrequently bilateral, so it is especially important that the scope of conservative surgery should be realized. Furthermore, they often occur in young women who have their child-bearing future ahead. Enucleation of such cysts is the operation of choice in young women. The operation is easy, tidy, and surprisingly bloodless. I have found diathermy helpful in stopping any slight oozing from the tumour bed.

Bonney (1937) has recorded cases similar to the above, and has emphasized that there are many ovarian conditions which, as a general rule, should be treated by conservative surgery.

Oxford. C. SCOTT RUSSELL, F.R.C.S.Ed., M.R.C.O.G.

REFERENCE

Bonney, Victor (1937). *J. Obstet. Gynaec. Brit. Emp.*, **44**, 1.

Estimation of Bromide in Body Fluids

The necessity may arise at intervals to check the administration of bromides or their mixtures to patients during a course of treatment. Particularly is this the case in a mental hospital. A suitable and easily worked process would therefore be an advantage, and the one described below is by no means complicated and gives fair results.

Not much work has been undertaken on this subject recently. Only one process for blood bromide could be found. This was by Barbour, Pilkington, and Sargant (*British Medical Journal*, 1936, **2**, 957). When testing this method in the hospital laboratory very poor results were obtained, although standard bromide solutions were employed. It was found that traces of serum protein unprecipitated from the first stage prevented the formation of the gold colour-combine. Further, sodium chloride in concentration equal to that obtained in blood serum similarly prevented the colour formation. Iodides gave exactly the same colour-combine as bromides when treated with the gold chloride solution.

It will thus be seen that these distracting features had to be eliminated before any reliance could be placed upon the results. The following process was therefore instituted.

1. URINE

A 24-hour sample of urine is collected and measured. 100 c.cm. of urine is evaporated to dryness in a silica basin on a water-bath. The urine is previously made slightly alkaline with 5% NaOH. Ignite slowly until all organic matter is decomposed, but do not continue heating to drive off all the carbon. Cool, and add about 10 c.cm. of distilled water and a few drops of 5% HCl till slightly acid; heat to almost boiling-point and filter. Wash with warm distilled water at least three times. Keep bulk of fluid as low as possible, if necessary by further evaporation. Transfer filtrate to a separator and cool. Add 10 c.cm. of chloroform ($CHCl_3$) and 5 c.cm. of freshly prepared chlorine water, shake vigorously, and allow $CHCl_3$ + Br to settle for a few minutes. Run the $CHCl_3$ layer into another separator under 10 c.cm. of distilled water. Treat the original solution with a little more $CHCl_3$, shake, and add to first $CHCl_3$ extract. Wash quickly with distilled water. Run the total $CHCl_3$ + Br extract into a separator, add 10 c.cm. distilled water, and slowly add just enough anhydrous Na_2CO_3, shaking the while until the red colour of the bromine in the chloroform disappears and the whole becomes water-clear. Shake well and allow to settle. The aqueous layer now contains NaBr in solution. Run off the $CHCl_3$ carefully. To the aqueous layer 1.5 c.cm. of a 1% gold chloride ($H.AuCl_4$) solution is now added, and drop by drop 5% HCl until the orange-red colour is fully formed. Three or four drops of the acid solution should suffice. This colour is then compared in a colorimeter with a standard NaBr solution of known strength (2 or 4 mg.). The appropriate quantity of standard should be diluted to the same volume as the final aqueous solution of the material under test, made slightly acid with dilute HCl, and 1.5 c.cm. of the gold solution added.

Test of Process.—4 mg. of NaBr was added to 50 c.cm. of a normal urine and the entire process carried out. 3.81 mg. of NaBr was recovered. Tests on patients receiving exact quantities of bromide daily showed an excretion of from 60 to 70% of the added salt over that period.

2. BLOOD

The process can be adapted to blood, a small measured quantity of which is incinerated slowly until most of the carbon is driven off. Further steps are then completed as above. It is most advisable here to keep the bulk of the liquid as low as possible. The results may vary slightly owing to the small amount of sample used.

It is not claimed that this process is 100% efficient, but with careful working comparative results will be assured. The chemical reactions made use of are of the simplest nature and, should it be desired, the test could be carried out in any laboratory.

Staffordshire Mental Hospital, Stafford. J. S. SHARPE, M.B., Ch.B.

Gaucher's Disease: Diagnosis by Sternal Puncture

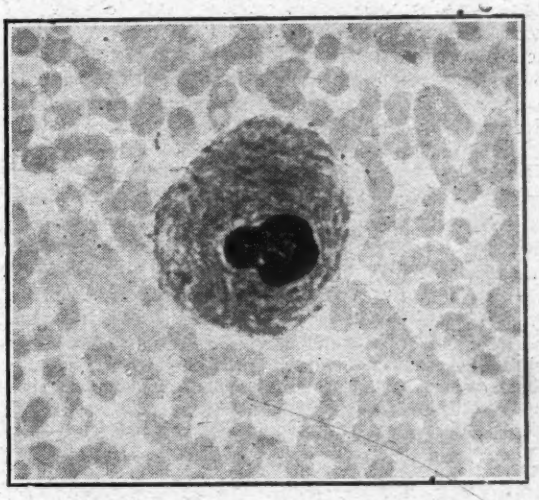
The case reported below was referred to me by the Armed Forces Medical Board on account of splenomegaly. The diagnosis of Gaucher's disease was made by sternal puncture. In view of the rarity of the condition and the fact that this case was revealed by the routine examination of recruits it is felt that a brief clinical memorandum would be of interest.

CASE HISTORY

The patient, a youth aged 19, is of British nationality and is not of Jewish ancestry. There is no familial history of splenomegaly. One brother died at birth. The father is at present on active service in the Royal Navy. The mother is alive and well, and apparently healthy. He has had no serious illness apart from an attack of bronchitis at the age of 10, though there have been occasional mild attacks of "influenza." During these attacks the patient feels a creaking sensation over the spleen.

Eighteen months ago the spleen was found to be enlarged when he was examined by his doctor during an attack of "influenza." Since then an increase in the size of the spleen has been noted. His general health is good and he has played rugby and water-polo without difficulty.

Examination revealed a tall, well-built youth of healthy appearance, with no conjunctival pingueculae or abnormal pigmentation. There was no abnormality of the nasopharynx or chest. The blood pressure was 130/85 mm. Hg. The spleen was enormously enlarged, with a firm edge and an easily palpable notch. In the supine position, at a point 2 in. lateral to the umbilicus the lower margin of the spleen was 6 in. from the costal margin. The lower thorax on the left side was visibly bulged forward by the underlying spleen. The liver was not palpable. There were no palpable glands apart from a few small slippery glands in the left axilla.



Investigations.—Blood count:—Hb 110% (Haldane scale); mean diameter of cells (halo method), 6.8 μ; red cells, 6,120,000 per c.mm.; leucocytes, 6,000 per c.mm.—polymorphs 56%, lymphocytes 40%, monocytes 4%; platelets, 285,600 per c.mm.; red cells stain normally. Bleeding and coagulation times were normal. Urine:—No protein of any nature present. Hippuric acid excretion test for liver function:—In one hour 17.4%, in two hours 47.5%, in four hours 82.6% of ingested sodium benzoate excreted. Red cell fragility to saline normal. Radiographs of skull, scapula, humerus, pelvis, and lower ends of femora showed no abnormality. Marrow smear:—After a prolonged search a typical Gaucher cell was found (see photomicrograph). Otherwise the picture was within normal limits.

Emanuel (1941) reported two cases of Gaucher's disease diagnosed by sternal puncture. In one, that of a man aged 30, the splenomegaly was revealed through the routine examination of recruits.

I am indebted to Prof. S. L. Baker and Dr. C. E. Jenkins for their interest and help, and to Mr. Gooding for his excellent photomicrograph.

M. L. THOMSON, M.D., M.R.C.P.,
Honorary Assistant Physician, Salford Royal Hospital.

REFERENCE

Emanuel, E. (1941). *Edinb. med. J.*, **48**, 843.

There were 25,285 persons on the register of the Pharmaceutical Society of Great Britain at the end of last year, compared with 25,224 the year before. The total includes 4,471 persons known to be serving with H.M. Forces. Since 1900 the number of pharmacists has increased by 10,000 and is now 1 to 1,800 of the population, compared with 1 to 2,700 in 1900. The proportion of women pharmacists is now 10.5%. Last year the number of women entering pharmacy was 52% of the total.

Reviews

BACKACHE AND SCIATICA

Backache and Sciatic Neuritis. Back Injuries, Deformities, Diseases, Disabilities. With Notes on the Pelvis, Neck, and Brachial Neuritis. By Philip Lewin, M.D., F.A.C.S. With drawings by Harold Laufman, M.D. (Pp. 745; 235 figures. 50s.) London: Henry Kimpton.

This work has been written for the general practitioner. To many the anatomy and mechanics, the investigation, diagnosis, and treatment of the spine when deranged or diseased is a closed book. And yet an enormous literature has been accumulated upon different aspects of these matters. It is a notorious playground of the charlatan. That an attempt should be made by such a distinguished orthopaedist as Dr. Lewin to "open this book" is timely. Yet he would have been more successful if he had been disciplined by even a little of the shortage of paper with which our medical writers have to contend. If "brevity is the soul of wit," so also conciseness and clarity are the essence of science.

Though well printed and illustrated on good paper it is very uneven in its teaching. There are some excellent chapters, particularly on the investigation of spinal disturbances and upon general matters of treatment. The whole is tinged with a naivety which will be somewhat strange to crusty old conservatives of Great Britain, and yet is often stimulating to those who understand American ways of thought and humour. Nevertheless the volume is clouded to a disturbing extent by verbose repetition. The work of other writers is freely quoted but often with lack of critical assessment and explanation such as the general practitioner really needs. An impressive bibliography is added as an appendix, but to a number of the items there mentioned we find no reference in the text, and, conversely, we found authorities noted in the text and no corresponding entry in the bibliography. The book seems to have been written in haste, with no proper editing, for how else could one have such repetitions as on page 439, where it is stated:

> "Pure sciatic neuritis is rare. It probably does not occur except . . . due to metallic poisoning, arsenic or lead, or to an infection or as alcoholic or syphilitic neuritis, as an avitaminosis or from anaemia. Sciatica may be due to diabetes, syphilis, alcoholism, lead poisoning, or any lesion producing an inflammatory or degenerative change directly in the nerve tissue." . . . "The predisposing factors in sciatic pain are congenital anomalies, postural defects and metabolic, circulatory, and endocrine disturbances. Determining factors are infection, trauma, exposure, and fatigue. Any focus of infection, exposure, etc., may precipitate an attack. Vitamin deficiency is also a predisposing factor."

This is not an isolated instance. It is also found, for example, on page 442 in an involved discussion upon the relation of the pyriformis muscle to the sciatic nerve. A section on page 471 on "Uncontrollable Brachial Neuritis" is entirely concerned with a proposal of Cushing's for the treatment of malignant spinal metastases with paralysis below the 12th thoracic segment by transection of the spinal cord. Further on we find, under "Chordotomy," a confused statement of the origin of the Spiller-Frazier operation. Discussing traumatic lesions of the sciatic nerve it is stated: "The order of return of function following *internal popliteal* (tibial) injury is: the gastrocnemius, tibialis posticus, *peronei, tibialis anticus*" (our italics). The last two mentioned muscles are later correctly listed under injuries of the external popliteal nerve; but an equally confusing and inaccurate statement had already been given on the page before.

Into the book has been dragged much material whose relation to backache is slight—e.g., burns and skin grafting, gas gangrene, anaesthetic and general surgical technique—and some irritating repetition in describing and enthusing upon the Kenny treatment of poliomyelitis. The lack of condensation and judgment, the insertion of inconsequential asides, and numerous inaccuracies produce an unfortunate atmosphere of confusion. Such errors shake our confidence in the book as a whole, and this confidence is not increased by reading the detailed and over-enthusiastic description of operations for ruptured intervertebral disks and spondylolisthesis, by inadequate illustrations of the radiological appearances of spinal lesions (e.g., spondylolisthesis), the intrusion of illustrations from the advertising literature of commercial firms, and a mere passing reference (and that Putti's) to the use of the plaster jacket in sciatica.

After reading the book and going back to Dr. Steindler's foreword it seemed to us still true that "even the most ardent advocates of surgery concede that backache is largely a problem for conservative treatment. . . . What we still need is to be shown how far rest can be accomplished by conservative means and when and why operative methods . . . become necessary." Dr. Lewin has, we feel, "just missed the boat."

THE CANCER PROBLEM

The Riddle of Cancer. By Charles Oberling, M.D. Translated by William H. Woglom, M.D. (Pp. 196. $3.00 or 20s.) Connecticut: Yale University Press; London: Oxford University Press. 1944.

In 1942 the book *Le Problème du Cancer*, by Prof. Charles Oberling, was published in the series "France Forever," in Montreal. On both sides of the Atlantic experts in cancer research recognized that here was a book which provides the balanced and exact information needed by medical students, by doctors who have not enough time and leisure to read original literature widely, and even by well-informed lay people. It is not primarily a book for those who are well acquainted with cancer literature, but even for the expert it provides ideas and novel analogies and subtle arguments which cannot fail to enlighten and broaden his conception of the vast problem which cancer presents.

Cancer research has now become so extended that it is almost beyond any one man's capacity to be master of all its branches; such a man would need to be very well acquainted with chemistry, bacteriology, genetics, parasitology as well as with pathology and general medicine. The mass of facts now accumulated about cancer—e.g., the induction of cancer by a hundred or more pure chemical compounds administered by feeding or injection or by mere inunction on the skin; the initiation of cancer by hormones, the influence of heredity, the action of viruses, the part played by Bittner's milk factor in mammary cancer—must necessarily cause confusion or lead to sterile argumentation unless the whole mass can be surveyed and correlated in a way which does not offend the general sense of the fitness of things. The key to the general survey is the pathology of cancer, and here Prof. Oberling is completely at home. He realizes as acutely as the early pathologists who disentangled cancer from granulomas, and the pioneers of cancer research—e.g., Bashford, Leo Loeb, Ehrlich, Borrel—that the problem to be solved is autonomous growth, a form of growth which is unique in pathology. Again and again in his discussions of the meaning of the many discoveries which have been made during the forty years of experimental cancer research, Oberling uses the pathological nature of cancer as the touchstone of importance. To review this book adequately would need more columns than any journal could possibly spare; all aspects of the subject are dealt with fully and fairly.

The French edition of this book was attractive not only because of the masterly way in which facts were brought together to form a rational picture of perhaps the most complicated disease process in the whole realm of pathology but also because of the elegant precision of the language. It must often occur to the English reader that our French colleagues have an advantage over us in the language they use. But it must be admitted by all readers of Dr. Woglom's translation that the English edition loses little or nothing of the grace and beauty of the original. Dr. Woglom deserves the thanks of the English-speaking world for giving us such a faithful and beautifully written volume.

TROPICAL MEDICINE

Tropical Medicine. By Sir Leonard Rogers, M.D., F.R.C.P., F.R.S., and Sir John W. D. Megaw, M.B. Fifth edition. Churchill's Empire Series. (Pp. 518; illustrated. 21s.) London: J. and A. Churchill. 1944.

That a new edition of this book has been called for within two years of the appearance of the fourth edition is perhaps not surprising in view of the increasing number of medical officers being drafted for service in the Tropics. The authors, as they say, have resisted the temptation to increase the size of the book by the incorporation of new matter. Such fur-

information as was necessary, particularly in the chapters devoted to malaria, kala-azar, trypanosomiasis, typhus, leprosy, and dietetics, has been introduced by the procedure of rewriting many pages in these sections. The upshot of this has been an actual reduction in the size of the book. To the casual observer it appears unchanged, but careful inspection shows that much new information of real value has been included, so that readers may rest assured that in it they will still find a thoroughly reliable and up-to-date account of all those conditions which are grouped under the heading "tropical diseases." The book was written originally for the tropical practitioner, and this objective has not been lost sight of; in this, the fifth, edition the medical officer who has to deal with patients in the Tropics will find all the information he needs, not only for treating the sick but also for maintaining in health those under his care. As with the earlier editions, the latest can be thoroughly recommended to all those, whether young and inexperienced or old and mature, who are called upon to practise medicine in the Tropics.

Notes on Books

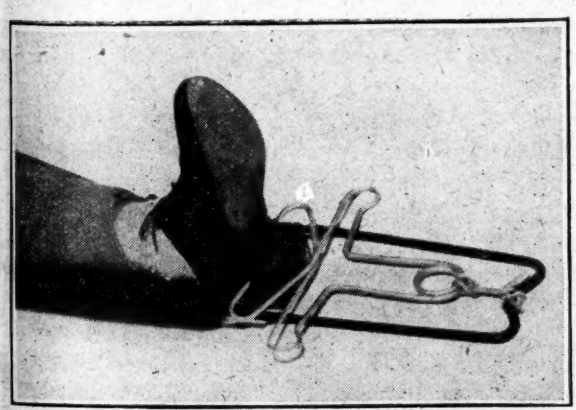
Lewis's Medical and Scientific Library, Gower Street, London, W.C., was founded in 1848 to supply mainly the needs of members of the medical profession and also to lend out books of scientific, technical, or philosophic interest not to be found in the ordinary circulating libraries. It has proved a boon to generations of medical students and practitioners and to workers in the allied sciences. The last full catalogue (to Dec., 1937) has been out of print for some time, and a Supplement covering the four-year period 1938 to 1941 is also out of print. A new edition has been revised to the end of 1943. Part I, "Authors and Titles" (714 pages), and Part II, "Classified Index to Subjects with Names of Authors" (208 pages) are issued together in one volume from 136, Gower Street (12s. 6d. to subscribers; 25s. to non-subscribers). Every book in Lewis's Library is the latest revised edition, and the aim of the catalogue is to provide subscribers with the titles of the works available there. For reasons of space and practical usefulness books for which there is no demand and textbooks which have passed out of date are withdrawn from time to time. The catalogue includes about 24,000 titles and it forms a very useful work of reference.

Preparations and Appliances

CLIP FOR USE WITH THOMAS SPLINT

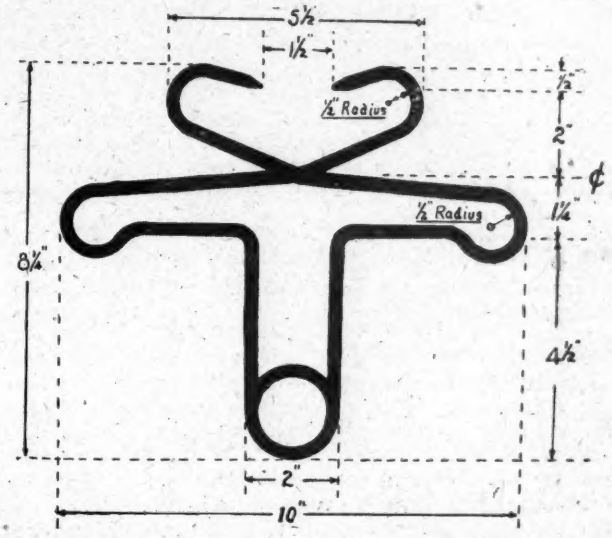
Mr. J. R. M. WHIGHAM, *M.C.*, M.S., F.R.C.S., writes from St. Andrew's Hospital, Bow, E.3.:

The accompanying illustrations show a clip for use with the Thomas splint which has proved valuable. It is made of 1/4 in. round mild steel and consists of jaws, wings, and tail. The jaws grip the side of the boot, the wings rest on the parallel bars of the splint and prevent rotation, and the tail when lightly held opens the jaws ready for application on the principle



of the towel clip. Extension cord can be attached either to the tail or to the wings. The more the pull on the wings the greater is the grip on the boot.

The grip resembles in some ways the Millbank pattern of Lieut.-Col. Monro, R.A.M.C., detailed in the *British Medical Journal* (Feb. 10, 1940, p. 217), but the addition of the tail gives the clip a handle and makes it, I think, easier to apply, especially under the difficult conditions which often confront the first-aider. A ready sling for the fractured limb can be improvised by passing the splint through the sleeve of a jacket, and this completes the essential treatment.



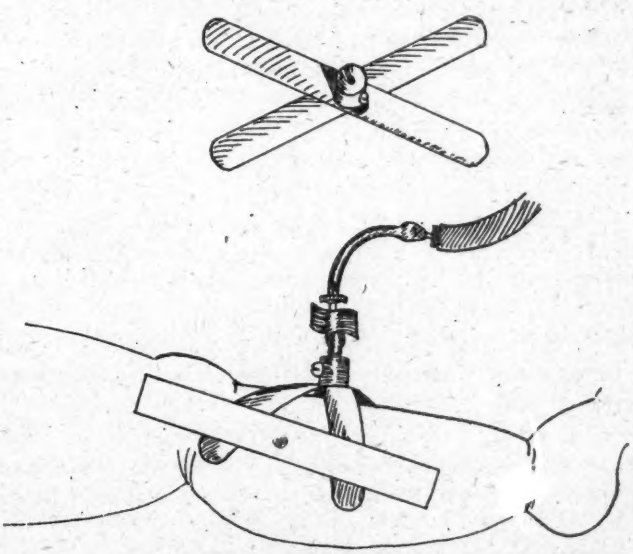
STEADYING GADGET FOR TOCANTINS'S NEEDLE

Dr. BRIAN V. I. GREENISH writes from the Grove Hospital (L.C.C.):

When using the longer types of Tocantins's needle for intramedullary drip therapy in the tibiae of infants, especially if treatment has to be continued for longer than 24 hours, the needle tends to become less stable than it is at first, due partly to its own slight top-heaviness, partly to contraction of the child's muscles, and partly, no doubt, to its unavoidable movement when the child has to be changed. On several occasions I have found this to lead to leakage of fluid back through the tissues, escaping where the needle penetrates. Mr. Delo, assistant hospital engineer, kindly made the following gadget to eliminate this fault.

It consists of two arms of a light, malleable metal (aluminium), joined at their intersection by a small brass collar with a hole large enough to slip the needle through it easily, and with a finger screw to secure the needle firmly. The joint is movable, so that the arms can be made to cross one another at any angle. The whole is sterilizable.

The needle, after the small collar supplied with it has been removed, is pushed through the collar and the finger screw is



tightened. The arms are straightened and the needle is pushed into the medullary cavity. The arms are then moulded round the child's leg and secured with adhesive plaster. The needle is thus firmly held, the efficiency of treatment is increased, and the child is relieved from the great discomfort of an unsteady needle.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY FEBRUARY 24 1945

INFLUENZA: WHERE WE STAND

Scrutiny of the epidemiologist's tables and charts can tell us much about the nature and behaviour of influenza, but vital statistics alone have not revealed and are never likely to reveal the whole story. Nor can we expect that study of the behaviour of influenza viruses in laboratory animals will, by itself, unravel the mysteries of the disease. There is urgent need for concerted attack by epidemiologist, clinician, and laboratory worker. Progress made by such correlated studies is reviewed in the first of Lieut.-Col. Stuart-Harris's Goulstonian lectures, published in our issue of last week. The yearly variations in the incidence of influenza take on a new significance when we know that the major peaks have been associated with the activity of influenza A virus, and that in years without pronounced peaks that virus has been rarely, if ever, isolated. Influenza A virus is now recognized to have been the causative agent of almost every one of the serious outbreaks all over the world since, in 1933, it was shown to be pathogenic for ferrets and thus became amenable to study in the laboratory. The serologically distinct influenza B virus, first recognized in 1940, has been recovered in a few wide outbreaks, sometimes in association with the A virus, but has not been proved to be a major cause of trouble; there is some evidence that it is more apt than is A to cause sporadic infections or to be associated with grumbling outbreaks not showing the sharp peaking which is characteristic of A epidemics. Virus A tends to make itself felt every other year; in this country it seemed liable to cause particularly large outbreaks every fourth winter. Thus it hit us in 1933 and in 1937. It was detected in the blitz winter of 1940–1, but, when we most feared it, the threatened outbreak came to nothing. Its next public appearance was in the winter of 1943–4, when it started a sharp outbreak in October instead of waiting till its favourite month of January. We understand that neither virus has yet been detected this winter.

Certain winters, as in 1934–5, 1938–9, 1939–40, and perhaps this winter also, have no major epidemic, but clinical influenza turns up in larger quantity than in other blank years; sometimes it is most noticeable in semi-closed communities, in outbreaks which do not spread generally. These "intermediate" years are particularly puzzling. Laboratory study shows that virus A may be present, but in a minority of clinical cases, and B may exist alongside it; but most cases are not obviously associated with either virus. Stuart-Harris discusses whether another strain of virus is at work here or whether modified strains of A or B are concerned. Whe virus A is recognized in such seasons it tends to be low virulence for ferrets, and the antibody response attacked persons is also of a lower order than in epidem years.

The second of the Goulstonian lectures, published this issue, deals with experimental evidence as to immuni to influenza and with the possibilities of active immuniz tion. Serological studies of human sera have been carri out on a large scale, especially since Hirst's discovery th influenza virus will agglutinate fowl and other red blo cells. This agglutination is inhibited by specific antise and this inhibition is the basis of a quantitative test whi can be carried out in any laboratory where fresh blo cells are available. It now seems clear that possession o high-titre antibodies does not guarantee anyone again getting an attack of 'flu, for the disease may assault peopl having antibodies at any level. There is, however, a te dency—no more—for influenza to lay low in larger num bers persons with relatively poor antibodies. This bein so, vaccination, which probably acts by raising antibod levels, will never guarantee an individual against infectio though it may appreciably reduce the incidence in a com munity. Virus inactivated by formalin and injected sub cutaneously has been the basis of almost all influenza vir vaccines to be tried; these have been improved lately b substituting for mouse-lung filtrates allantoic fluid fro infected chick embryos. Such material contains muc more virus and less unwanted protein than preparation used earlier. Concentration by several methods can b applied to improve the product still further. Unfortunatel evidence suggests that even the best vaccines have a effect on immunity of comparatively short duration, pe haps a couple of months. A recent trial in America, whic Stuart-Harris mentions, gave much the best results ye recorded—approximately a fourfold reduction in incidenc of clinical influenza; but, as he says, "it may well b . . . that the extraordinarily successful timing of vaccin tion, which was in fact a matter of chance, was an impo tant factor in the success of the experiment." For in th trial the outbreak began at just about the time when th response to the vaccine was at its height. At present, whe we cannot foretell just when an epidemic is coming, would be wasteful, if not actually harmful, to inject infl enza vaccines indiscriminately, on the off-chance of epidemic's appearing when the resulting immunity was s raised. The alternative course, though administrative difficult, seems much wiser at present—namely, to pla laboratory-trained scouts to look out for evidence activity by viruses A and B and to distribute a inject the appropriate vaccine as rapidly as possi when the scouts' reports indicate that the right mom for doing this has come.

A recent report by Friedewald suggests that, by mixtu with suitable adjuvants, an influenza vaccine will produ much better and more prolonged effects: this work has n yet reached the stage of clinical application, but its furth development may ultimately solve some of our difficulti Meanwhile we do well not to look only to vaccines banish influenza from our midst. Far more do we n

to learn all the grisly details of the natural history of the virus. The factors permitting epidemics to arise are certainly complex. One of them is the cyclical variation in the immunity of the herd, high after an outbreak, gradually falling till the next one begins. Another concerns the whereabouts of influenza A virus between epidemics. It has but rarely been incriminated as a cause of sporadic influenza. Was there any special significance in its appearance in scattered local outbreaks in the summer preceding the October–December, 1943, epidemic? Is it ever brought to our shores from abroad? Can the virus lie hid in some other host, as swine influenza has been shown to do in the pig lung-worm and earthworm? If the chain of causation of influenza epidemics proves to have many links we may hope all the more to find one of them which is not too hard to break.

Stuart-Harris touches but lightly on the crucial but highly speculative question of the relation between ordinary A outbreaks and pandemics such as that of 1918–19. In a recent and fascinating review of pandemic influenza Shope[1] says: "We may be missing something of significance in the epidemiology of influenza by placing our entire confidence in the conception that every case of influenza, especially at the outset of a pandemic, must of necessity spring from some preceding case of the disease." Discussing the autumn wave of 1918, he points out the difficulty of explaining on the basis of contact infection "its relatively slow diffusion over comparatively short distances as compared with its unbelievably rapid spread over geographically wider areas." It is gratifying that Stuart-Harris sees no signs suggesting that a pandemic visitation is threatening the final stages of World War II. We devoutly hope he is right.

TREATMENT OF LARYNGEAL CANCER

The treatment of carcinoma of the larynx has fascinated laryngologists and surgeons for some ninety years, since Garcia made the living vocal cords visible in the laryngoscope. In the early days it could not be expected that the disease would often be diagnosed in its initial stages; consequently any rational treatment by surgery had to be adapted to at least moderately advanced cases, but if not radical enough it was naturally disastrous, while if conceived on a scale appropriate to the extent of the disease its mutilating character carried the seeds of disaster in the magnitude of the plan. Of the many who laboured to overcome the technical difficulties Gluck above all others succeeded in converting the story of failure from all kinds of septic complications, of which he has given a careful historical account,[2] into one of the most satisfactory chapters in the tale of surgery for carcinoma. Without going further into historical detail it may be said that the evolution of laryngeal surgery has now produced a reasonably safe operative technique appropriate to every stage of intrinsic cancer, so long as it remains intrinsic. Laryngofissure, modified hemilaryngectomy, and total laryngectomy (now by the aid of chemotherapy almost freed from risk in otherwise sound subjects) provide a standardized technique applicable to all the varieties of situation and extent of the disease, and it is unlikely that much further technical progress will be made in this direction. The less mutilating of these procedures, suitable for early cases, provides nearly 80% of cases free from recurrence for ten years; while total laryngectomy in more advanced cases, where the cancer is not only more extensive but often changing in character to a more malignant type, provides 60% of ten-year cures.[3] Nevertheless it is only natural that, for an organ so intimately connected with the functions of voice and respiration and deglutition, efforts should be made to cure the disease by radiotherapy without subjecting the patient to the hazards and mutilation associated with surgery. If these efforts are to be justified, however, they must show results at least as good as may be claimed for excision. The direct application of radium to the growth, or as near as possible to the base of the tumour, was the method first adopted, and with various modifications it still finds favour in the practice of some who like to combine surgery with radiation; but radiation applied from a distance in the form of deep *x*-ray therapy or by beam from a large quantity of radium has also been given extensive trial and with some measure of success.

Using radium needles applied to the base of the growth by removal of part of the laryngeal cartilages Harmer[4] reports that of 24 early cases 14 survived three years, and of 72 more advanced 32 patients are still living. This gives percentages of 58 and 46, which are inferior to the results of surgery. Lederman and Mayneord[5] in a study of the distribution of radiation from teleradium in the larynx by different techniques showed by physical measurements how these techniques can be adapted to individual needs, while when radium needles are used as the source of radiation the distribution in the horizontal plane shows a region of heavy irradiation principally at the anterior commissure but falling off rapidly along the cord towards the arytenoid cartilage. Morton, Gray, and Leary[6] have also found, by measurement of the dosage reaching the area of the vocal cord and its environment, that by the usual method of employing needles the anterior part of the larynx receives twice the dosage that reaches the posterior part. Therefore, unless the tumour is very small, complicated methods of application are needed to ensure a homogeneous dose throughout a tumour which has extended much either along or below the vocal cord, and homogeneity of dosage is one of the guiding principles for this form of radiotherapy. It may be that a method of applying needles in conformity with this principle will be devised, but the method generally adopted hitherto gives one reason why treatment with needles so often fails except in very early cases where the growth is small. In any event there is no means of telling beforehand

[1] *Medicine*, 1944, **23**, 415.
[2] Gluck, Th., and Soerensen, J., *Geschichte der Operationen am Larynx und Pharynx*, Vol. IV, *Handbuch der speziellen Chirurgie des Ohres und der oberen Luftwege*, Katz, L., Preysing, H., and Blumenfeld, F., Würzburg, 1911–14.
[3] Colledge, L., Roy. Soc. Med., Discussion on Treatment of Carcinoma of the Larynx, Feb. 2, 1945 (in press).
[4] Harmer, W. D., ibid.
[5] Lederman, M., and Mayneord, W. V., *Brit. J. Radiol.*, 1943, **16**, 301.
[6] Morton, J., Gray, L. H., and Leary, G. J., ibid., 1944, **17**, 204.

whether an epithelioma will prove to be radio-sensitive or radio-resistant, but for needling a rigid standardized technique must be applied. It might be expected, therefore, that high-voltage deep *x*-ray therapy or treatment by teleradium would have certain advantages, both in the matter of distribution of the dosage throughout the volume of tissue to be irradiated and in enabling the treatment to be adapted to the progress of the case by observing the local reaction to the radiation. In fact both Nielsen and Strandberg[7] (Copenhagen) and Max Cutler[8] (Chicago) have gone so far as to recommend a therapeutic test in order to discover whether the tumour is radio-sensitive, in which case a full course of treatment is administered, or whether it is radio-resistant, so that if the response is unsatisfactory the case may be transferred to the surgeon. This assumes, however, that the radiotherapist will have the moral courage to abandon his line of treatment in midstream, as it were, and such an Olympian level of reasoned pessimism is not to be expected of every radiotherapist. However, Lederman[9] can show by the use of teleradium the following results at the Royal Cancer Hospital: out of 8 early cases 6 remain free of symptoms, and of the other two patients, who also became free of symptoms, one died from intercurrent disease and the other is untraced; out of 15 more advanced cases (i.e., suitable for laryngectomy) 12 patients are living and free from symptoms, 6 of them for more than five years. This appears to indicate a clear superiority over treatment by needles, though the figures are still small.

The position at present therefore remains that surgery can give as good results for laryngeal cancer as for any other situation favourable for surgery. Not only is biopsy useful surgically in confirmation of the diagnosis, but Broder's grading provides a fair indication of the degree of malignancy and therefore of prognosis from the surgical standpoint, though at present histology gives no information on the matter of radio-sensitivity. If a surgical line of treatment is chosen much attention must be devoted to selection of the appropriate operation. There should be no exploratory laryngofissures. If the choice of treatment falls upon radiotherapy—which may often claim an advantage in the case of the aged and of those who nowadays are described, regardless of grammar, as "poor surgical risks"—then a decision has to be made between (*a*) the local application of needles, with economy of radium but erratic dosage and some risk of wound infection, and (*b*) irradiation at a distance by deep *x*-ray therapy or by teleradium, with accurately distributed dosage, absence of operative risk, and the opportunity for observing the progress of the case during treatments. It is useless to deny that the introduction of radiotherapy has enveloped the whole subject in a fog of prejudice and bias; and the best that can be done for any individual patient is to place him in the care of someone who has had a comprehensive experience of both lines of treatment and is capable of deciding what is the best treatment for the particular case, or in the care of a surgeon and a radiotherapist who are really willing to co-operate.

[7] Nielsen, J., and Strandberg, O., *Acta radiol.*, Stockh., 1942, **23**, 189.
[8] Cutler, M., *Arch. Otolaryng.*, Chicago, 1944, **39**, 53.
[9] Lederman, M., Roy. Soc. Med., Discussion on Treatment of Carcinoma of the Larynx, Feb. 2, 1945 (in press).

PRECOCIOUS FEMALE PUBERTY

If every physician were first to say to himself: "It depends what you mean by 'precocious,'" many an infant belly would remain unscarred. That there is a great variation in the time of onset of puberty among perfectly healthy girls is obvious. It is not so obvious at what stage it is justifiable to believe that the onset is early or late enough to warrant a search for a cause. Climate and race are certainly factors to be considered. Puberty at 9 is unusual in Northern European peoples, but would certainly not be considered abnormal in southern or tropical races. Are we justified in regarding as deviations from health even such extreme cases as that of Lina Medina, the Peruvian girl who began to menstruate at 7½ months and created a world's record by giving birth to a child when only 5 years and 8 months old?[1]

The constitutional element is one which has been neglected by many workers. The onset of puberty depends, so far as present knowledge goes, on two factors—the production of oestradiol by the ovary, presumably as a result of pituitary stimulation, and the response of the tissues to this ovarian hormone. That the latter factor is variable, not only between individual and individual but between one part and another of the body of an individual, and even between the right and left sides of the individual, is well recognized. It seems impossible to escape the conclusion that the response of a girl's tissues to oestrogenic stimulation is, as Novak[2] has put it, part of "an underlying foreordained sex pattern innate in the human mechanism and having its source in the chromosomes themselves." If this is so we must expect to find wide variations in the age of onset of puberty in the absence of any discoverable endocrine cause. A disorder of the endocrine system may be expected sometimes to cause an abnormality in time or in strength of the necessary oestrogenic stimulus, but it cannot affect the underlying susceptibility to stimulation of the tissues of the body. In fact, a tumour as a cause of precocious puberty is rightly suspected but seldom found. A tumour of the adrenals, which may cause precocious puberty in boys or virilism in girls, is a very rare cause of true female puberty. Reilly and his colleagues[3] were able to find only 4 reported cases. Pineal tumours, on which great stress was formerly laid, produce true precocious puberty only in boys, and it is now accepted that they do so not by virtue of any endocrine overactivity but by pressure upon the hypothalamus. Lesions in this area, tumours of the tuber cinereum and corpora mammillaria, hydrocephalus, and encephalitis have been occasionally reported as causing true female precocious puberty, probably by interfering with the functional control of the anterior pituitary. Of greater numerical importance is the granulosa-celled ovarian tumour. Lull[4] was, however, able to collect only 16 reported cases of precocious puberty due to this cause. Even so, the patients are not strictly pubertal, for their "menstruation" is in reality oestrogen-withdrawal bleeding, and ovulation is lacking.

In a recent review Novak[2] has emphasized the rarity of neoplastic cases (one in 60,000 patients passing through the department of gynaecology of Johns Hopkins in 60 years), and has emphasized the relative frequency of the constitutional type hitherto neglected by the majority of workers. How common such cases are it is impossible to say, for different observers have used different criteria of precocity, and many cases have doubtless gone unreported or have been reported without full investigation.

[1] Escomel, E., *Presse méd.*, 1939, **47**, 875.
[2] *Amer. J. Obstet. Gynec.*, 1944, **47**, 20.
[3] Reilly, W. A., Lisser, H., and Hinman, F., *Endocrinol.*, 1939, **24**, 91.
[4] *Amer. J. Obste .Gynec.*, 1941, **41**, 445.

As an index it is noteworthy that Novak has never encountered a neoplastic case in his own practice, but here reports 9 cases, 6 of them his own, in which the investigation and subsequent history make a constitutional diagnosis inevitable. The age of the first menstruation in this series varied between 15 months and 7½ years, the arbitrary age at which children were excluded from the series being 8.

The prognosis of the constitutional type of precocity is good. The girls grow into normal adults, except for a tendency to stunting of the long bones due to early union of the epiphyses. Their psychological management may be difficult, and it must be remembered that they ovulate and may, like the young girl of Peru, become pregnant.

EMOTIONAL ALBUMINURIA

Like the systolic heart murmur, albuminuria is a call for critical attention rather than a sign of disease. Benign albuminuria, which occurs in the absence of organic renal disease, is a well-known condition which is quite common in adolescents and young adults. It is frequently orthostatic, the albuminuria being associated only with the erect posture. It also occurs in almost everyone after violent exercise, and is not uncommon in students before examinations and in other conditions of mental strain. The factor of emotion in the production of benign albuminuria has recently been given prominence by Ahronheim's observations[1] on a large group of men between the ages of 17 and 26 years who were potential air cadets in the United States Air Corps. The routine procedure included the examination in each case of two specimens of urine obtained within a period of 15 minutes, the second specimen being voided after the routine withdrawal of blood for a Kahn test. Albuminuria was present in practically all "fainters"—those who either fainted or showed shock-like symptoms and felt sick. In the whole group more than 50% showed albuminuria, of which the majority had a positive reaction only in the second specimen. A detailed follow-up was not possible, but it was calculated that the albuminuria was persistent in only about 2%. Ahronheim showed that there was a direct relation between emotion and the occurrence of the albuminuria, and he made the rather comforting if indefinite observation that in 50% of an unspecified number a considerable albuminuria cleared promptly when the subjects were given a draught of medicine which had the properties of being bright and bitter.

In considering the pathogenesis of emotional albuminuria a clue is provided by the very high incidence in the "fainters," in whom there were the usual signs and symptoms which document gross vasomotor disturbance. It is known that in animals even transitory interference with the arterial or venous supply to the kidney produces albuminuria.[2] In the orthostatic type the alteration in posture probably produces albuminuria as the result of a transient renal circulatory disturbance. It is therefore not difficult to accept as a likely factor in emotional albuminuria a transient change in the blood flow of a similar nature, an effect of the widespread vasomotor disturbance associated with syncope. Although the translation of the psychic disturbance into terms of vasomotor changes is probably mediated through the hypothalamus, there is no reason to suppose that a close parallel exists between emotional albuminuria and the so-called cerebral albuminuria of acute brain injury. Acceptance of the view that benign albuminuria is common carries with it the assumption that the glomerular capillary membrane is often permeable to plasma protein under conditions which are within the range of experience of the normal individual and the normal kidney. The facility with which protein can pass through the glomerular capillary wall is in keeping with the trend of recent work by Whipple[3] and others,[4 5] which suggests that there is a much freer and more rapid passage of protein between the circulating plasma and the protein stores of the tissues than is suggested by the orthodox view that the capillary wall is relatively impermeable to plasma protein.

[1] *War Med.*, 1944, **5**, 267.
[2] Fishberg, A. M., *Hypertension and Nephritis*, 1939, 4th ed., p. 110, Philadelphia.

PROBLEMS OF INANITION

The study of inanition is one of great interest to both clinician and physiologist. In certain medical and surgical conditions lesions in the intestinal tract often interfere with the digestion and absorption of food, and some degree of inanition results. If this goes on long enough the patient may die. To some extent life can be prolonged by parenteral feeding with glucose, amino acids, vitamins, and emulsified fats, although such therapy is still experimental; the only substances in routine use are sodium chloride, glucose, and blood products such as plasma. We still do not know enough of the nutritional requirements in inanition. Holt and Kajdi[6] have thrown some light on the subject by noting the survival times of rats fed on water and single foodstuffs only. Rats have an uncanny skill in making dietetically sound selection of food. When offered a variety of pure foods they choose those suitable not only for optimal growth but for optimal calorie intake as well. Holt and Kajdi therefore assumed that in inanition the rat will eat only what it can make use of, and that its survival will indicate its need for particular foods made available to it. Survival was longest on a protein diet. Rats fed on fat or carbohydrate alone showed a gradual loss of appetite beginning towards the end of the first week and continuing progressively until death. This was attributed to lack of some dietary factor or factors concerned in the utilization of fat and carbohydrate. Rats fed exclusively on fat, carbohydrate, and protein diets drank widely varying quantities of water, the most with protein and the least with fat. The greater need for water on a pure protein diet is explained by the increased quantity of urea formed; it must have water for its excretion.[7] The "water-sparing" property of carbohydrates and fats is of some practical importance, particularly in conditions in which the intake of water is restricted either for therapeutic reasons or because of actual scarcity. Pronounced variations in survival rates were also observed with different carbohydrates. The best results were obtained with glucose, fructose, maltose, cane sugar, and invert sugar, which were almost identical in effect. On pentoses, lactose, and galactose survival rates were lower.

The gradual failure of appetite in rats given carbohydrate and fat to eat was attributed to an impairment of the utilization of food. In further experiments Holt and Kajdi[8] showed that deficiencies of the fat-soluble vitamins and minerals played no part in the phenomenon. Vitamin B_1 deficiency developed regularly in the third week of the tests, but there was no evidence of a deficiency of any other factor of the vitamin B complex. The most serious—namely, a deficiency causing failure of appetite on the third or fourth day—is apparently the want of some factor needed for making use of carbohydrate and fat. At present its nature is unknown. It may be some undiscovered food factor, or the protein component of some enzyme, which cannot be synthesized when the diet is lacking in protein.

[3] *Physiol. Rev.*, 1940, **20**, 194.
[4] Beattie, J., and Collard, H. B., *British Medical Journal*, 1942, **2**, 507.
[5] Sharpey-Schafer, E. P., and Wallace, J., *Lancet*, 1942, **1**, 699.
[6] *Johns Hopk. Hosp. Bull.*, 1944, **74**, 121.
[7] *Amer. J. Dis. Child.*, 1936, **52**, 751.
[8] *Johns Hopk. Hosp. Bull.*, 1944, **74**, 142.

THE PROPHYLAXIS OF TRENCH FOOT

BY

RAYMOND GREENE, D.M., M.R.C.P.

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In every war in history trench foot has been a serious cause of casualties. In the last great war there were 84,670 such casualties in the British Army. In the week ending Dec. 16, 1916, there were 3,104 cases in France and Flanders alone. One blizzard in November, 1915, caused 15,900 cases in Gallipoli and 988 in Serbia. After 1916 the incidence fell rapidly. It was realized that trench foot is almost completely preventable.

The present spell of mild weather following a hard frost is ideal for the production of this malady, and the time seems appropriate for a summary of the teaching which has been given to a large number of medical officers of the three Services in the war medicine courses at the British Postgraduate Medical School of the University of London.

Given proper training and good equipment, the incidence of trench foot is an index of discipline. It is the army in retreat, low in morale and with its communications in disorder, that suffers most severely. In other circumstances, it is almost as foolish to get trench foot as to blow off one's big toe with a rifle. There are bound to be unexpected circumstances in war to make the occasional case unavoidable, but when once an epidemic has been controlled every case should be the subject of inquiry. Almost every such inquiry will bring to light an error in training, equipment, or discipline which, checked in time, will save not merely sections or platoons but even brigades and divisions.

There is a way of life in cold damp weather which must be learned not only by medical officers but by combatant officers and by every individual man. The maintenance of cold-weather discipline must be the responsibility of the combatant officers, but it is the duty of the medical officer to see to it that his brother officers understand the reasons for the rules, and are continuously alert for breaches of them. In the battle against cold there is no place for "toughness." The man who breaks the rules and gets away with it is not a hero but a lucky fool. Moreover, he is a stumbling-block to those who are less well adapted, and he should be treated as a criminal.

Preliminary Training

In the training of troops it should be remembered that the physiological reactions to cold, which are the concern of the adrenal medullae, the thyroid, and the autonomic nervous system, are themselves capable of being trained. In those habitually overclad they become dulled. Troops should accustom themselves to exercise for short periods in the minimum of clothing in the coldest weather. In safe surroundings no more clothing should ever be worn than is necessary to prevent shivering. It is probably not necessary to emulate the Finnish custom of "wallowing naked in December snows," but bathing in cold water and drill in frosty weather stripped to the waist are both of great value.

Clothing

Sir Thomas Lewis showed that if the whole body is chilled the local protective reactions against cold may fail. The clothing must be as nearly as possible waterproof, for it is the great thermal conductivity of water which is to blame for trench foot. It should also be windproof, so that the protective warm layer of air about the body is not too often blown away. The clothing should be in many light layers rather than a few heavy ones, for the air caught in the interstices is of more value than much wool.

All clothing must be loose, for the essential cause of tissue damage in trench foot is the exudation from damaged capillaries, and the slightest venous constriction raises the intracapillary pressure to a serious degree. For this reason puttees were discarded. The boots must be loose, supple, well oiled, and preferably without toecaps. Socks should be undarned, and also loose. Most men can realize that tight boots are dangerous: they forget that tight socks are equally so. They forget, too, that though it is a good thing to wear two pairs of socks if the boots are large enough to take them, it is dangerous if they are not. Ideally the outer pair of socks should be a size larger than the inner, but this is a refinement usually impracticable. Garters and sock suspenders should be forbidden, the socks being kept up by pinning them to the pants. Gloves also must be loose. Some people favour an inner glove of thin silk covered by a woollen one, with a big outer glove of waterproof material. Personally I have always found an ordinary woollen glove perfectly satisfactory and the silk one unnecessary. The outer waterproof glove is important. It should be made without separate fingers and should be loose enough to slip on and off easily when fine finger movements are needed.

Damp

Dry extreme cold is far less to be feared than damp slight cold. Trench foot has occurred in temperate climates even in the spring. For this reason it is absolutely necessary that wet clothes, especially boots, socks, and gloves, should be changed at every opportunity. Combatant officers are sometimes inclined to regard such an instruction as "soft": they must be overruled. A general routine order issued to British Armies in France in November, 1915, laid it down that every man should carry a second pair of socks, and that where possible battalion arrangements should be made for socks to be dried and reissued during each tour of duty in the trenches; and that while in the trenches boots and socks should be taken off from time to time if circumstances permitted and the feet dried, well rubbed, and covered with dry socks. Although much more is now known of the pathology of trench foot, it is almost impossible to improve on this general routine order and the later Fourth Army standing order of June, 1917. Obviously the one extra pair should be increased to several whenever possible. Even if the boots cannot be dried, dry socks are a considerable protection.

The provision of gum boots for use in waterlogged trenches is important, but it must be remembered that sweat is itself dangerous, and gum-boots are sweaty things. Men must not march far in them. In the last war it was usually possible to arrange for men going forward for a tour of duty in waterlogged trenches to call at a post where they removed their boots, performed foot drill, and put on dry socks and gum-boots. On their return they left their wet socks and gum-boots, again performed foot drill, and donned their own dry socks and boots before going down the line.

Foot drill was performed in pairs. Each man washed the feet of his opposite number in warm water and carefully dried them. He then, in the early part of the war, rubbed in whale oil, but it was later found that the oil was unnecessary and a powder of talc and camphor was substituted. The benefit of the whale-oil treatment probably rested in the rubbing. All abrasions were reported to the medical officer. A double washing with ordinary and special soap was ordered, but this is probably an unnecessary refinement. A single wash with ordinary soap is probably as good. Foot drill should be performed in cold weather, both in and out of the trenches. A good method of drying boots is to lay a 6-foot length of gas-pipe across a brazier, push one end into the toe of a boot, and blow air from the other end with a bellows. If the business end of the pipe is made like a toasting-fork many pairs can be dried at once. These measures were often regarded as fussy, but the proof of the pudding was in the eating. The incidence of trench foot fell dramatically after the winter of 1915–16.

Stagnation

After constriction the most important cause of increased intracapillary pressure and consequent oedema and tissue damage is venous stagnation. The men must be taught not to stand still, slumped into their boots, but to keep the muscles of their calves continuously in motion. They must lie down whenever possible, with their feet higher than their heads—a manœuvre which lowers venous pressure. They must not sit on seats, boxes, or firesteps in such a way that the popliteal space is constricted. They must on no account bring their feet near to a fire if they are cold or numb, but warm them between a companion's hands or inside his clothes. The boots must be unlaced or, better, removed at every opportunity and at least twice a day.

Food

The warming power even of cold food is considerable, and men in danger of trench foot must be kept well supplied. Hot food is, of course, far better. Arrangements must be made by means of heat-insulated containers, self-heating tins, or such devices as "Tommy's cookers" for a regular supply of hot food and drink to men in exposed situations.

Trenches

The design of trenches in mobile warfare is easy to neglect, but is neglected at peril in time of thaw. Whenever possible they must be properly drained, or, as a second best, provided with duck-boards. Men cannot stand long periods in damp trenches. Commanding officers may be well aware of this in theory, but they may suffer from a wishful faith in the capacity of their own men to "rough it out." Such faith is always misplaced. Human physiology is remarkably adaptable, but it is not infinitely so. No equipment, however good, no precautions, however studious, and no watchfulness, however devoted, will avail if men have to spend more than 24 or at the most 36 hours in a waterlogged trench or fox-hole. If the prosecution of the war demands that men should fight in such conditions, then the High Command must allow for a high proportion of casualties. It is unreasonable that allowance should be made for casualties from firearms and not from the equally predictable hazard of cold. This hazard has not gone with the thaw. It has rather increased and will remain with the armies till summer comes.

AVIATION MEDICAL RESEARCH

AIR MARSHAL WHITTINGHAM'S ADDRESS

On Jan. 31 Air Marshal Sir Harold Whittingham, Director-General of the R.A.F. Medical Services, was presented with the John Jeffries Award of the Institute of Aeronautical Sciences of the U.S.A. We print below some extracts from his speech in acknowledgment of this honour.

Liaison across the Atlantic

Early in 1939 I had the privilege and pleasure of visiting the United States to see the high-lights of aviation and its associated researches. I visited 12 States, and was particularly impressed by the fine work done at Wright Field, in Dayton, by Col. (then Capt.) Harry G. Armstrong. I returned to the United Kingdom determined to build up so far as was in my power an aviation medical research organization much on the lines of Wright Field, where the aeronautical engineers and other scientists worked as a team with those engaged in the physiology of flight. The urgent problem was to fit the machine to the man, instead of the other way round, as had so long been the case owing to insufficient co-operation between the engineering and medical groups. That was a defect which this Institute has done much to eradicate.

Since 1939 there has been the closest and happiest liaison between British and American research centres and workers, both Service and civilian, including your National Research Council. To our mutual benefit, members of research groups from both countries have visited each other, and continue to do so, to study and discuss various problems at first hand. Thus on either side of the Atlantic and in the field, America, Britain, and Canada have pooled their knowledge and resources in aviation medicine to improve the comfort and efficiency of those engaged in flying during training and on operations.

Some Problems Investigated

Among the problems investigated, roughly in order of their occurrence, have been the following:

How to provide an adequate supply of oxygen, with the maximum of comfort, at all oxygen-requiring heights under the most adverse conditions.

How to protect air-crew against cold and the occurrence of frost-bite, which has now been reduced to negligible proportions (1 case in 2,000 bomber sorties—that is, 1 case in 12,000 individuals engaged in these sorties) by the provision of suitable clothing, particularly electrically heated garments.

How to prevent blacking out in combat during high acceleration without interfering with pilot-readiness, active movements, and performance under all climatic conditions.

How to guard the eyes against the glare of the sun and search-lights without reducing the field of vision or visual acuity, and how to obtain and maintain the optimum night vision under various flying conditions.

How to deal with such stratosphere problems as the prevention of bends, the physiological requirements in pressure-cabin design and development, including explosive decompression and bailing out from aircraft at altitudes over 30,000 feet.

How to lessen fatigue, which is such a potent factor in the causation of air accidents.

How to improve intercommunication, as poor intercommunication leads to fatigue and many errors, especially during the height of air operations.

How to protect those in cockpits and cabins of aircraft against the possible entry of noxious substances, such as exhaust gases or hydraulic fluids.

How to prevent air-sicknesss, particularly among paratroops.

Evacuation of Casualties by Air

In addition a considerable amount of research and development has taken place in connexion with air-sea rescue, and last but not least the evacuation of casualties by air.

The U.S. Army Air Force has done a stupendous job in evacuating casualties by air from all fronts to oversea bases and to the United States. Major-General David N. Grant, your Air Surgeon, deserves the greatest credit for this wonderful achievement, as he does also for the gigantic strides that your country has made in aviation medicine during this war.

The British endeavour, as regards evacuation of casualties by air, has been less only in proportion to the Forces employed. In 1944 the Royal Air Force alone evacuated approximately 300,000 cases of sick and wounded, mostly Army personnel, on all fronts—the Far East, the Mediterranean, and in Europe proper—without a single mishap, although this evacuation involved some 20,000 separate flights, and much of the flying was done from forward landing strips near the enemy, over jungle, mountain, and sea in all sorts of weather.

Outstanding Pieces of Work

I should now like to pay tribute to certain medical men of both countries who have done outstanding work for aviation. Some of our theoretical calculations of the effects of stratosphere flying on man have proved to be wrong; certain hazards were overstressed, others were underestimated, with resulting casualties.

In 1941, during the experimental phase of adapting the Boeing 17 for operational work at higher altitudes, two R.A.F. medical officers —Squad. Ldrs. W. K. Stewart and J. Robson—had the misfortune to be in one of these aircraft when it broke up at an altitude of some 32,000 feet. Stewart was the sole survivor.

Col. Randy Lovelace, of the U.S. Army Air Force, in 1943, purposely and courageously bailed out at 40,000 feet to make physiological observations in a parachute descent from such an altitude. He became unconscious almost immediately after bailing out and suffered severe frost-bite of the hand, but fortunately landed safely. Only last year another distinguished American research worker, Col. Boynton, met his death doing an experimental delayed parachute drop from 44,000 feet, though he knew the hazards. He was a very brave man and a great loss to science.

Again, Squad. Ldrs. Gibson, Pask, and Stewart carried out a series of dangerous experiments—to find out how long man could live during a parachute descent without additional oxygen—in rarified atmospheres similar to those between altitudes of 44,000 and 25,000 feet. These laboratory experiments were carried to just short of extremes and gave valuable information to help perfect apparatus and technique for bailing out in the stratosphere.

In studying the problems of high acceleration in aircraft, that brilliant young American scientist Lieut.-Cmdr. Lillienkrantz met his death tragically some two years ago.

In the Royal Air Force Squad. Ldrs. W. K. Stewart and S. Davidson have carried out since 1940 many hundreds of blacking-out experiments in the air, having to bail out from damaged aircraft on more than one occasion. Squad. Ldr. Davidson has also for the past year been engaged in experimental flying on jet-propelled aircraft to study various physiological problems. In this connexion it is of interest to note that some 120 R.A.F. medical officers are qualified pilots, many being highly skilled—flying Spitfires and even jet-propelled aircraft.

Many medical officers have made physiological and psychological observations during actual air operations against the enemy to assess the strain, fatigue, behaviour of air-crew, and general efficiency of

the flyer and his equipment. Thus, in 1942, that gay, lovable Highlander, Group Capt. Hugh Corner, was shot down in his Spitfire by a Messerschmitt over the English Channel when studying what he called "mental lapses" of members of Paddy Finucane's Fighter Squadron.

Wing Cmdr. Roland Winfield has done some 50 operational sorties to study aviation medicine problems in bomber and coastal aircraft on all fronts. Wing Cmdr. MacGown has won the coveted Pathfinder badge, studying night-vision problems over Berlin and other enemy targets.

To assess the flotation value of life-jackets for the unconscious man Squad. Ldr. E. A. Pask had himself anaesthetized for a total period of 3¼ hours, while he was thrown into a swimming bath in different positions, wearing various types of life-jackets. Many of these jackets were so designed as to ensure drowning of an unconscious man. Of the types he tested, the British Mae West, the New Zealand Navy, and the German life-jackets proved to be the most efficient and to give adequate flotation. A film of these tests was shown to all concerned, and most of the defects have now been remedied.

In conclusion, I would like to stress that these advances on aviation medicine have been accomplished only by the full co-operation of aircraft instructors, aeronautical engineers, medical men, physicists, physiologists, and textile experts of the United States of America, Britain, and the Dominions working in the closest liaison. Long may this association for our mutual benefit endure in peace as in war.

ROYAL COLLEGE OF SURGEONS

RESTORATION AND DEVELOPMENT FUND

There must be many Members of the Royal College of Surgeons of England and other medical men and women who are interested in the effort to make the College a still more worthy headquarters of surgery in this country. We therefore reproduce below a personal letter which the President, Sir Alfred Webb-Johnson, Bt., sent on Feb. 14 (John Hunter's birthday) to each of the Fellows of the College, asking for their support for the Restoration and Development Fund.

The President's Appeal

The time has come when we must prepare for the restoration of our College. The sum which will be received from the War Damage Commission will not cover the whole cost of restoration; moreover we have a unique opportunity to carry out many improvements which will make our College an even more worthy headquarters of British surgery. Among the amenities which it is proposed to provide are a large Conference Hall, common rooms, extensions of the museum and library, accommodation for the new professors, and more research laboratories. It is estimated that £250,000 will be required to complete the scheme of development. In order to have a free hand in planning, and, at the same time, to provide space for the sister colleges if they decide to move to Lincoln's Inn Fields, the Council has acquired several adjoining properties.

The future scientific influence of the College has been assured by the generous endowments we have received from Sir Buckston Browne and the Bernhard Baron Trustees, and from our latest and greatest benefactor, Sir William H. Collins. I now appeal to Fellows of the College for donations to the Restoration and Development Fund. I realize that commitments vary for all of us, and that many of us have suffered considerable financial loss owing to the war, but I want every Fellow to feel that he has made some contribution towards making our College worthy of its progressive outlook and great history and traditions.

Past and present members of the Council and Court of Examiners have subscribed over £10,000. The appeal has been supported by the American College of Surgeons, the Royal College of Surgeons of Edinburgh, the Royal College of Surgeons in Ireland, and many surgical associations. Donations can be earmarked for special purposes and can be spread over a term of years. If a gift is intended for the scientific departments a seven-years covenant can be entered into with the result that the benefit to the College will be greatly increased. I rely on you to help as generously as possible.

R. N. Herson, G. P. Christopoulos, and N. F. Coghill (*J. R.A.M.C.*, 1944, **83**, 107) record their observations on 432 cases of mumps occurring between November, 1942, and the end of April, 1943, principally in Cypriot troops stationed in Cyprus, and representing part of an epidemic in the island at that time.

Reports of Societies

PENICILLIN: USES AND LIMITATIONS

A discussion on the uses and limitations of penicillin took place at the Medical Society of London on Feb. 12. The president, Dr. ANTHONY FEILING, was in the chair.

Sir ALEXANDER FLEMING said that penicillin was received for use as a yellow powder. Pure penicillin was in white crystals; the yellow denoted impurity. With penicillin were administered a number of impurities, the composition of which was not known, and which varied according to the methods of extraction and manufacture. Originally it was said that the sodium salt only could be injected, but with the higher standard of purity of the material which had now been reached this was no longer true; the calcium salt could be used for all purposes, and it had one advantage over the sodium salt in that it was not so deliquescent. One important thing about penicillin was that it was non-toxic to leucocytes. The ordinary antiseptics like carbolic acid killed the leucocytes more quickly than they killed micro-organisms. Penicillin was reputed to be bacteriostatic, but it was being established that it did kill micro-organisms and helped to dissolve them. He showed a table dividing the organisms which were sensitive and insensitive to penicillin:

Sensitive	*Insensitive*
Staphylococcus	B. pyogenes
Streptococcus (except enterococcus)	B. proteus
Pneumococcus	B. influenzae
Meningococcus	B. pertussis
Gonococcus	B. pestis
Diphtheria bacillus	V. cholerae
Anthrax bacillus	Friedländer's bacillus
Morax-Axenfeld bacillus	Enterococcus
Gas gangrene bacillus	Tubercle bacillus
Tetanus bacillus	
Spirochaetes	

Penicillin must be brought into contact with the micro-organism. The expensive way, though the easy one, was to inject it so that it got into the blood; the cheaper but more troublesome way was to put it on to the infected area so that it reached the organisms locally. In injecting penicillin into a vein the administration must be repeated because the kidney excreted it very rapidly. With the intravenous method, using the standard dose of 15,000 units, most of the substance had disappeared within an hour. With intramuscular injection it remained for about two hours; if 50,000 units were given, for rather more than four hours, and, if 100,000 units, for rather more than six. Intravenous drip was the most economical method of using penicillin, but it involved certain troubles, while as to intramuscular drip, there was a limit to the amount of fluid which could be put into a muscle with comfort to the patient, but subcutaneous drip served the purpose quite well. The latest apparatus for introducing the requisite small amount of fluid was one in which a small clock or motor worked a spindle in such a manner as to turn a screw once in an hour, and this was connected with the piston of a syringe so that up to one million units, or something like ten times the ordinary dose, could be given subcutaneously in 24 hours without discomfort.* The stock dose of penicillin was 124,000 units in 24 hours given either by single injections or by drip. His clinic had been successfully using half that dose when the ordinary sensitive organisms, like the staphylococcus and the streptococcus, were concerned. With less sensitive organisms the dose had been larger.

Dramatic Effects of Penicillin in Gonorrhoea

The treatment of generalized infection caused by any of the sensitive micro-organisms could be undertaken with success, and when penicillin became plentiful Sir Alexander Fleming had no doubt that this would be done. Cases of staphylococcal septicaemia, which formerly were regarded as almost hopeless, now all but invariably got well. In venereal diseases the effect of penicillin was dramatic. Gonococcal infection seemed the

* See *British Medical Journal*, Jan. 27, 1945, p. 122.

easiest of all to get rid of by means of the drug. The stock treatment at the moment was 100,000 units split up into 8 or 10 doses given at 2- or 3-hourly intervals. This seemed to cure something like 97% of the cases. Such frequent repetitions were not administratively so suitable for civilians as for those in the Services, and in the case of civilians the plan was often followed of giving 100,000 units in the morning and 50,000 at night, and it seemed to serve the purpose, though it was probably not as good as the frequently repeated administration throughout the day. Syphilis was now being placed on the list of diseases to be treated with penicillin. A start was made by giving 120,000 units for a week in the usual split doses; this had since been doubled, but even with the smaller dosage the spirochaetes disappeared in from 12 to 15 hours. The Wassermann reaction became negative, and the patient appeared well, though in some cases there was relapse, and he was a bold man who would declare that he could cure syphilis with anything.

Oral and Respiratory Infections

Penicillin was likely to be extremely successful in the region of the mouth and the respiratory tract. Nearly all the micro-organisms common in these regions were sensitive to penicillin; the only trouble was to get the penicillin into contact with them. He did not know how to get penicillin into a sinus, but most sinus infections were due to penicillin-sensitive organisms. He mentioned one case of fractured jaw which was expected to become septic. Penicillin was given for 4 days, and the wound healed without sepsis. Penicillin if injected into the blood did get into the meninges, though not in high concentration.

The two serious limitations of penicillin were its instability and its rapid excretion. When made up in the form of solutions, ointments, creams, or lozenges (he was sure that when it became plentiful there would be enormous quantities of penicillin lozenges used for the less serious mouth infections) it was unstable. If anybody could invent a method whereby it was not rapidly excreted this would simplify the treatment very greatly. Some would say that it was a further disadvantage that it could not be given by the mouth, the acid in the stomach destroying it; that, however, might be an advantage in preventing its abuse. Great care had to be exercised in making it up to see that it was bacteriologically sterile, otherwise something might be produced with it which would destroy the penicillin, and what was administered would not be penicillin but a culture of the organism which had destroyed it. But if care were taken over these details there was in penicillin something nearer to the ideal antiseptic than had ever been known before.

"The Surgeon's Occupation Gone"

Mr. A. DICKSON WRIGHT said that penicillin was an antiseptic which went beyond all the dreams of the bacteriologist. In the last war Sir Almroth Wright was always looking for an antiseptic which would kill micro-organisms and would not kill the leucocytes, and they now saw how right his quest had been. Here was something which worked in a concentration of 1 in 50 million, which was equivalent to 1 drop in 550 gallons. In one sweep all the infections of the skin and all the infections of the airways were almost brushed aside by this one antiseptic. "We are only left now to discover something for the alimentary tract, and then we are through." The surgeon's occupation would be gone. It was true that he might have still to deal with collections of pus, but in this war, in which penicillin had been used with great liberality, large collections of pus were not found. Boils and carbuncles had been simply "wafted away." Osteomyelitis, which was a busy field for the surgeons, would presently be closed to them entirely. Pyaemic arthritis and pyaemic infections of the joints would be brought to an end. The ear, nose, and throat surgeon would find fewer occasions for his intervention. In urinary conditions Mr. Dickson Wright had seen stubborn staphylococcal infections of the urinary tract swept away by penicillin. Wonderful results had been recorded in the treatment of gonorrhoea. Childbirth fever might be expected to disappear. Post-operative infections were nearly always staphylococcal, and the use of penicillin would save many a patient from disappointment and complaint and many a surgeon from chagrin. In orthopaedics large operations on the hip were very prone to develop staphylococcal infections, and these would now be under control. As for dentistry, he imagined that in all future extractions a prophylactic dose of penicillin would be given. In Vincent's angina penicillin gave miraculous results. Within 24 hours the most vicious and firmly entrenched "Vincent's" had all the "kick" taken out of it. He had seen a large carbuncle of the lip, giving the patient acute misery, lose all its venom within 24 hours. So far as virus diseases were concerned, apparently nothing was claimed for penicillin, though he believed it had been used and found of value in psittacosis. When the chemistry had been worked out he felt sure that some method would be found of linking penicillin with a radicle, as had been done with insulin, to delay its absorption. Penicillin had "opened a vista which leaves us reeling." One thing was certain: surgeons were going to lose a great deal of their work, and the people were going to enjoy a tremendous benefit.

Dr. A. HOPE GOSSE said that empyemas had been found to be "penicillin-sensitive." In some cases, if the empyema had been diagnosed quite early before thick pus had formed, the fluid seemed to clear up without drainage. He described also three cases of acute nephritis treated with penicillin, all of which did well.

Baffling the Imagination

Mr. ZACHARY COPE said that in the case of staphylococcal septicaemia penicillin was "simply wonderful." It baffled the imagination to think what would follow the full development of this drug. Surgery was being revolutionized before their eyes, and the young men entering surgery now would have a very different outlook from their predecessors, concerning the reaction of the tissues and the like. He desired to ask Sir Alexander Fleming how often skin irritation of any kind occurred after using penicillin, and also his view concerning the reaction of penicillin in endocarditis. He himself had for years felt that there was a great deal which still remained to be understood about the reaction of the cellular tissues. He also asked what delay in the onset of syphilis had been noticed in certain cases after the clearing up of a gonococcal infection.

Mr. V. E. NEGUS referred to the use of penicillin in oto-laryngology. One of the great bugbears had been a fulminating sinusitis affecting a patient suddenly after swimming. Recently he saw a naval officer who, after a swim, developed a condition of severe staphylococcal septicaemia. He was treated with penicillin, and five days later he saw him at his military hospital taking part in a dance, whereas, without this treatment, his chances of being in his coffin by that time were considerable. Another patient developed a mediastinal abscess, with a temperature of 105°, and would have died, but was cured very quickly with penicillin.

Dr. C. E. LAKIN asked whether it was possible to mix oil with penicillin so as to diminish the rate of absorption. Dr. G. W. GOODHART asked whether there was any evidence that the absence of leucocytosis in the blood had any bearing on the question of penicillin treatment. He mentioned two cases of staphylococcal septicaemia in which there was an extremely low leucocyte count. Dr. L. CARLYLE LYON asked whether any patients were known to be allergic to penicillin, also whether penicillin was useful in the tertiary stage of syphilis.

An "Umbrella" for Operation

Mr. E. W. RICHES said that the organisms infecting the urinary tract—*B. coli*, for example—were not sensitive to penicillin. In his unit for spinal injuries he had seen a number of patients who had penicillin from the beginning, and it had not, of course, prevented urinary infection altogether. There was not a drug at present known which would entirely prevent infection. But penicillin had been extremely useful in helping to clear up cases in which the infection was mainly staphylococcal, and it had been used as an "umbrella" under which to operate in cases of stone formation and had helped to tide such cases over a difficult period.

Mr. R. C. BROCK said that in thoracic surgery they were looking forward to great benefits from penicillin, in particular in the after-care of pneumonectomies.

The PRESIDENT wished to take the opportunity of testifying to the remarkable effects of penicillin in many germ infections. He had seen, at a neurosurgical unit, a number of these cases, the result of gunshot injuries of the brain, and the value of penicillin there had been demonstrated. The surgeons sewed up the wound completely within a short time and no sinus infection developed later. He mentioned one recent case of a man aged 48 admitted to hospital with clear signs of meningitis. Lumbar puncture gave a turbid fluid. He was put on sulphathiazole. The culture showed a pure pneumococcus. Pneumococcal meningitis, particularly if no primary cause was discoverable, was accompanied by a high mortality even after the sulphonamide drugs were available. In this case the sulphonamide was continued, but the patient had two intrathecal injections of penicillin on two successive days, and got perfectly well and left the hospital within a week; he could hardly be persuaded to stay as long as that. Dr. Feiling mentioned two cases in which penicillin had failed. One was a staphylococcal septicaemia in a woman of nearly 70 who died in spite of continued intramuscular drip, and in whom post mortem no bacterial endocarditis was found. He had also tried penicillin, quite experimentally, in a very severe case of glandular fever, with continued high temperature and a most violently inflamed throat, both tonsils being very much enlarged, with a superficial necrosis on one tonsil. The penicillin gave no benefit, though the patient did recover spontaneously within about a week.

Sir ALEXANDER FLEMING, in reply, said that it was interesting to hear about the use of penicillin in glandular fever. If the micro-organism of glandular fever were known it would come within the insensitive category. That was the sort of case in which he would not expect a good result. Concerning skin irritation, this did occur sometimes, though not often, and was never serious. He had seen an American report concerning urticaria, but this seemed to occur with the use of pure penicillin, so that it was not to be attributed to one of the impurities. The Americans had made certain claims concerning the value of penicillin in endocarditis, but he himself had not much faith in the short-term treatment of that condition. In endocarditis penicillin had to diffuse into the "vegetation," and a certain concentration in the blood was necessary for a considerable period. Before long they might be expected to know more about the treatment of endocarditis by doses of 5 million units which was projected in America.

A question had been asked about the use of penicillin in the form of snuff. This was much more pleasant in the form of dried plasma with penicillin, and he was told that in some more or less acute nasal conditions it was a treatment worth trying. Endeavours had been made to delay the absorption of penicillin by means of oil, and one mixture was of an oil containing 5% of beeswax. This did seem to delay the absorption, but there were troubles in its preparation and injection.

He could only with difficulty answer the question about delay in the onset of syphilis. Air Cdre. McElligott had told him recently that he had had several cases where syphilis was delayed, after treatment for gonorrhoea, for from 60 to 80 days. As for the treatment of tertiary syphilis, he must refer the questioner to the American journals, for nobody in this country had experience of it. In the U.S.A. they had been using penicillin for general paralysis of the insane, and he had seen one report which stated that it was as good as malaria treatment.

Mr. Dickson Wright had suggested that surgery was going to disappear. That, of course, was an exaggeration. On the other hand, the use of penicillin would take away one at least of the surgeon's disabilities, for he need no longer wear a mask while operating.

Approximately 2,400 newspapers and periodicals were examined last year by the Law Department of the Pharmaceutical Society of Great Britain and its inspectors for advertisements, now forbidden, of "cures" for certain diseases. In many instances the Society had the advertisements amended without taking proceedings. A number of infringements were, with the consent of the Attorney-General, brought before the courts.

Correspondence

Nursing in Tuberculosis

SIR,—Much of the "tuberculophobia" which still exists and which is exhibited by some of your correspondents is surely based upon shibboleths which die a hard death. There is still little distinction drawn between infection by the tubercle bacillus, which is universal, and tuberculous disease, which is relatively uncommon. And there is very little appreciation even among those who should know better, of the essential difference between the innocuous manifestations of primary infection and progressive phthisis. The sanatorium nurse—that much-photographed, much-investigated scapegoat for prejudice—is certainly infected during the course of her duties but no one, in spite of every effort, has been able to convict her of undue tuberculous morbidity. To be sure, the sanatorium nurse does not claim an *ex-officio* immunity to disease, and a certain number of young women prove to be unfavourable reactors. In this case there is always some bystander who will cry havoc.

The figures of Hansen of Oslo have been mentioned by Dr. W. E. Snell (Feb. 10, p. 198), but Ustvedt, summarizing the work of all the Scandinavian workers in this field (with particular reference to intensive investigations in connexion with infection and disease in hospital nurses), states:

"Infective dose and virulence are factors which we can disregard . . . The type of bacillus may possibly play some part in countries where bovine tuberculosis is prevalent. . . . The role of superinfection has not been fully elucidated, but it cannot be regarded as all-important. . . . It therefore appears that on the whole the widely varying course of the tuberculous infection in different individuals can only to a very slight degree be regarded as dependent upon variations in the infection itself. We must turn to the infected organism to find the explanation."

It should be remembered that no other comparable group of young women is submitted to such physical, mental, and psychological strain as is the hospital nurse, and that her conditions of work often leave a good deal to be desired.

Ustvedt, Jacobs, and other writers have also pointed out fallacies in the popular conception of the significance of "massive infection" as a factor in the aetiology of tuberculous disease. Of far greater value is the growing appreciation of the significance of environmental factors in aetiology, and particularly of genetic factors, as demonstrated in the recent remarkable work in the United States on the incidence of tuberculosis in twins.

Those who continue to speak of sanatorium nursing as a hazardous undertaking should await the publication of the close analysis of the health of sanatorium nurses which is promised by Drs. Edwards and Clark Penman (Jan. 20, p. 957), and of other reports which are in process of preparation.—I am, etc.,

Harefield County Hospital, Middlesex. L. E. HOUGHTON.

Solubility of Sulphadiazine

SIR,—In the leading article on sulphamerazine (Feb. 3, p. 155) it is stated that the solubility of sulphadiazine is 139 mg. per 100 c.cm. at *p*H 7.6. From the preceding sentence this presumably refers to solubility in urine. The figure quoted differs from the figure given in M.R.C. War Memorandum No. 10 on "The Medical Use of Sulphonamides," in which it is stated that the solubility in urine at 37° is 52 mg. per 100 c.cm. It is important to know which figure is right.

If the patient is taking 4 g. sulphadiazine a day, then, assuming 75% of this is excreted in the urine unchanged, there will be 3 g. in the urine. If the urine has a *p*H of 7.5—that is to say alkaline—the volume required to dissolve it will be 6 litres or 10 pints, if the solubility is 52 mg. per 100 c.cm. Since few patients excrete so much urine as this, many must suffer from deposition of crystals in the urinary tract. If, however, the solubility is 139 mg. per 100 c.cm. the same amount of sulphadiazine will be excreted in 2.2 litres, or 4 pints. This is a very different story.—I am, etc.,

Department of Pharmacology, Oxford. J. H. BURN.

*** The figures given for the solubility of sulphadiazine have varied somewhat in different papers. Thus in the original

description by W. H. Feinstone, R. D. Williams, R. T. Wolff, E. Huntington, and M. L. Crossley (*Johns Hopk. Hosp. Bull.*, 1940, 67, 427) the solubility is given as 12 mg. per 100 c.cm. in water at 37° C., 32 mg. in urine at *p*H 6.6, and 107–247 mg. in blood. D. R. Gilligan and N. Plummer (*Proc. Soc. exp. Biol.*, N.Y., 1943, 53, 142) give a curve from which it can be deduced that the solubility is 100 mg. per 100 c.cm. at *p*H 7.2, about 223 mg. at *p*H 7.5, and about 270 mg. at *p*H 7.6. In the paper by L. H. Schmidt, H. B. Hughes, E. A. Badger, and I. G. Schmidt (*J. Pharmacol.*, 1944, **81**, 17), which supplied the figures to which Prof. Burn refers, the solubility is given as 41.6 mg. per 100 c.cm. at *p*H 6.8, 78.5 mg. at *p*H 7.2, and 130 mg. at *p*H 7.6. However, all these authors are agreed that the solubility is comparatively low in acid solution and that it is greatly increased if the solution becomes slightly alkaline. It is understood that the figures given in the M.R.C. Memorandum were based on the earlier publications and that they will be revised in the second edition (now being prepared) according to the fuller information now available.—ED., *B.M.J.*

Painful Intramuscular Injections

SIR,—Dr. Geoffrey Dean (Dec. 2, 1944, p. 737) doubts if it is universally recognized how painful intramuscular injections of penicillin can be. It is not in fact widely recognized because intramuscular injections of penicillin are not invariably painful. Since, however, patients do suffer acute pain, which can be avoided by simpler means than Dr. Dean suggests, it might be well to examine the contributory factors in detail. These factors are the same as for any intramuscular injection—namely, (1) The skill of the operator. (2) Efficiency of instruments. (3) Nature of skin antiseptic. (4) Nature of substance injected. (5) Position and attitude of patient. (6) Patient's threshold to pain.

1. Patients requiring penicillin now and for some time to come must be hospitalized, and therefore the operator for these 3-4-hourly injections is a senior nurse. It is inevitable with day and night staffs and changes for off duty, etc., that a fortunate patient will have at least three operators in any 24 hours. The liability to pain varies with the training and skill of the nurses, and in particular the variation is most marked in the rate of insertion of the needle and the rate of injection of solution. The inexperienced pierce the skin slowly (and painfully) and proceed to inject rapidly, giving rise to a particularly unpleasant stinging pain of wide radiation. Contrariwise the injection which is virtually painless results from a bold insertion of the needle and a slow (2 c.cm. per minute) rate of injection of solution. This speed of the procedure is the most important single factor in the production of pain.

2. The period of penicillin injections during the past two years has been one in which the quality of steel allocated to needle manufacturers has deteriorated, and thus the life of the cutting edge of a needle is shorter and requires more care—e.g., the routine replacement of the stylet between use so that the projecting end prevents contact with, and injury by, other metallic objects.

3. Spirit has become almost the only skin antiseptic in general use for injections, intramuscular and intravenous, and for artificial pneumothorax. It is a common experience that some patients complain of pain when submitting to injection of material other than penicillin where this antiseptic is used. This pain is due in most instances to the irritant action of spirit carried from the skin by the needle to the soft tissues, and can be avoided by using ether or ether meth. and allowing a few seconds for evaporation before inserting the needle.

4. It is recalled that many parenteral therapeutic agents—e.g., liver extract, arsenicals, etc.—have been painful when first introduced, due to unsuitable *p*H and/or contained impurities. The use of local analgesic is an uncertain method of minimizing pain in these cases and converts a simple procedure into one which is complicated and time-consuming.

5. Recent letters in your columns have debated the respective advantages of the buttock and the lateral thigh area, though no reference has been made to position—upright or recumbent. When the injection is made into the buttock in the upright position the usual practice is to have the patient unsupported. If, however, the subject is allowed to lean on the edge of the desk or couch the glutei are relaxed, and as a result perhaps more long courses of treatment involving this method might be completed! In the bed-patient the gluteal injection is usually given when the patient is lying in the half-lateral position, so that it is made in an awkward vertical direction. Apart from other important considerations, the external vastus site is far more convenient, and makes an injection in the horizontal direction easier and less liable to pain.

6. Apart from the recognized variation of individuals in their pain threshold there is the patient's variation at different stages of the illness. This, as well as other points mentioned above, is clearly exemplified in the following account:

A patient suffering from a staphylococcal septicaemia had a total of over 4,000,000 units of penicillin during various periods aggregating some nine weeks in a five-months illness. In the first few desperate days he was hypersensitive to handling of any sort, and penicillin injections by all but one (expert) person provoked a "refusal of treatment" reaction. This short period ended by an improvement in general condition and by the substitution of ether for spirit as a skin antiseptic. Injections were continued, and maintained due to relapse, for a period of eight weeks, and the ruthless monotony of 3-hourly day-and-night injections became a small factor in the patient's comfort provided the skin was cleaned with ether, the needle sharp, and the injection made slowly.

After a remission of two months injections were resumed for one week, when 2 c.cm. (20,000 units) of penicillin was injected 3-hourly. There was no comparison at this stage with the condition of the patient at the beginning of the illness, and during each of the last 50 or so injections he didn't "turn a hair." He did, however, turn his head if a blunt needle necessitated two attempts to pierce the skin or if the rate of injection was raised! No local analgesic was used throughout, and the majority of injections were made laterally into the upper two-thirds of the thighs.

In view of the increasing use of the intramuscular route more training should be given to nurses and junior medical officers in the details of this procedure, and care should be shown in the selection of nurses delegated to give the injections. It is not enough to order therapy for a patient suffering from a severe general infective condition which will probably require a protracted series of injections for recovery, and to be satisfied if nurses whose aseptic technique and training are not fully established are left, eager but nervous, to undertake injections which may result in the disaster of a broken needle. It is not necessary to acquire all skill on human beings; there is the post-mortem room for doctors and the tennis ball (when obtainable) for nurses; and in any case for both there are the opportunities presented by the occasional single injection or the short series prescribed for conditions of local infections.—I am, etc.,

WM. DODD.

Injectable Liver Extracts

SIR,—In your issue of Feb. 10 (p. 197) Dr. Harold Fullerton called attention to the danger attending the use of injectable liver extracts that possess little or no potency. This is clearly a matter of much importance. I am strongly in favour of immediate steps being taken to obviate any such danger.

I suggest that this might be achieved by making it a compulsory requirement that every issued batch of injectable liver extract shall have been shown to have produced a satisfactory response when the dose recommended has been administered to not fewer than three cases of pernicious anaemia that have not been previously treated or are in relapse. This, however, does not involve an accurate standardization such as is implied by stating the activity in units. The use of the term "unit," as applied to medicinal substances, is inappropriate except where an exact determination of potency can be made, in comparison with that of a standard stable substance which has been rendered available for this purpose. This is surely not the case with injectable liver extracts, since the only known method of testing them is the administration to a patient.

To all pernicious anaemia patients presenting themselves for curative treatment there is an obligation to administer sufficient injectable liver extract to ensure a good haemopoietic response. Without an almost unlimited number of suitable cases, one cannot determine the degree of curative activity with the accuracy required for expressing it in units. On the other hand, it is quite possible to determine that a given number of c.cm. administered to patients will produce a satisfactory increase in the red blood cells in 10 to 14 days. This being determined on every batch in at least three typical cases may be taken to pro-

vide a sufficient assurance that the extract in question possesses full activity. It does not, on the other hand, justify attributing to it a numerical value in terms of units.—I am, etc.,

London, N.1. FRANCIS H. CARR.

? Otitic Barotrauma

SIR,—The writer of your annotation on barotrauma (Feb. 10, p. 190) rightly asserts that "aero-otitis media" was a misnomer. "There is," he writes, "no inflammatory change . . . and therefore in the interests alike of accuracy and euphony the term otitic barotrauma has now taken its place and has been adopted by the R.A.F."

I do not want to argue about the euphony, but does the writer not realize that "otitic" signifies as much inflammation as "otitis," and that, therefore, the term "otitic" barotrauma is just as inaccurate as its predecessor? Will Air Cdre. Dickson and his fellow workers be prepared to write "otitic" ganglion when the otic ganglion is referred to? If we assume that similar events could occur in the stomach, we might, in the absence of inflammatory changes, speak of "gastric barotrauma." "Gastritic barotrauma" entails no less inflammation than "aero-gastritis."

The term otic (or aural) barotrauma avoids the pitfall; but, while the condition is certainly not "otitic," it is also very doubtful whether it is "traumatic" in the usual medical sense of the word. I maintain that "tubo-tympanic pressure syndrome" (which I suggested in a discussion at the R.S.M., *J. Laryng.*, 1943, **58**, 493), while of doubtful euphony, designates the condition more accurately.—I am, etc.,

London, S.W.12. A. B. ALEXANDER.

Selenium Poisoning

SIR,—In your issue of Feb. 10 (p. 196) you report a meeting of the Nutrition Panel of the Food Group of the Society of Chemical Industry on the effect of diet on industrial poisoning. To me is attributed a reference "to work on selenium poisoning in which, by means of labelled molecules, it has been shown that selenium took the place of sulphur in the methionine molecule, and hence caused what might almost be described as a conditioned protein deficiency." I fear that the reporter in a laudable attempt to condense my discursive remarks has attributed to me something that I did not say. I have already had one inquiry for the reference to the work to which I am reported to have alluded. To the best of my recollection, this was what happened. In the course of the discussion a speaker mentioned the selenium poisoning of cattle and the theory (not his own) that this might be due to its substitution for sulphur in the sulphur-containing amino-acids of proteins. In my remarks I called attention to some recently published work by du Vigneaud and his colleagues, in which it has been shown by the use of labelled elements that the sulphur of methionine is required for *in vivo* conversion to cystine, whereas the carbon chain of methionine does not appear in the cystine molecule. Putting the theory and the fact together, I suggested the possibility that selenium might thus interfere with the *in vitro* synthesis of cystine. But there is no experimental evidence for this purely speculative view, nor, so far as I am aware, has any biological work yet been carried out with labelled selenium.—I am, etc.,

Greenford, Middlesex. A. L. BACHARACH.

Choline for Fatty Livers

SIR,—I have read with interest the article by Drs. Alexander and Eiser (Sept. 30, 1944, p. 425) and the letter from Dr. Lewes (Oct. 28, p. 575) on infantile diarrhoea and vomiting. In 1939 Martin Hynes and I were working on this problem when a milk salesman put me on to some work by Wilkinson, Best, *et at.*, done, I think, at Liverpool, the gist of which was, that if rats were fed on a "fatty-liver-producing" diet they could be protected against getting fatty livers by the addition of protein to their diet. Impurities in the protein were found to be the active agents, choline being the one ultimately named. A fatty liver being so constant a post-mortem finding in this disease, we thought to protect our patients from it by giving them choline. Choline was difficult to get, but a preparation was found. The war intervened before a series could be treated in this way. I am certain the prevention of the fatty liver, if this is possible, will improve the prognosis, and suggest that choline may be a means of doing this. With this in view it would be interesting to know the choline content of the hydrolysates used at Southend.—I am, etc.,

Germany. R. E. BONHAM-CARTER, Capt., R.A.M.C.

Breathing and Coronary Circulation

SIR,—My letter published on Jan. 6 (p. 27) might have been written especially for members of the medical profession, for the death rate among doctors is 40% higher than among bank officials in the same social group. "Surgeon" (Jan. 20, p. 97) is to be congratulated on being treated so skilfully by Dr. A. T. Todd, who advocates breathing with the mouth open and when standing. The patient when breathing should be seated—all the muscles of the body should be relaxed, even the facial muscles; the shoulders should be held gently back and down, by the muscles acting just below the scapulae, 3 in. below the axillae. Mr. F. Matthias Alexander (author of *Constructive Conscious Control of the Individual*) would state that the relaxation of the chest muscles is important using only those previously mentioned, otherwise the range of movement of the thorax would be impeded. The first exercise is to breathe fully in and out deeply through the nostrils, the shoulders being first drawn back and down; the second is to inhale fully and then hold the breath for 15 to 60 seconds or longer; and the third is to exhale completely and then hold the breath for 15 to 60 seconds or longer. By keeping the shoulders down and back when standing, sitting, writing, and stooping, the necessary movement of the chest is carried on unconsciously, and the same happens at night, when lying, say, on the right side if the left elbow is placed just behind the long axis of the body. When standing the weight of the body should be on the balls of the toes. This way of breathing, besides helping the heart, is a wonderful restorative to all the remaining organs of the body.—I am, etc.,

Ealing, W.5. R. HALSTEAD DIXON.

Impetigo

SIR,—Surg. Lieut. J. Munro Gold's memorandum on impetigo treated by sodium penicillin (Feb. 3, p. 152) was extremely interesting, but I think calls for some comment.

1. He found acriflavine 1/2 gr., tannic acid 20 g., and water to 1 oz. unsuccessful. To my mind the failure was probably due to the fact that the lotion was too strong—half the above strength might have shown good results.

2. Failure occurred when ung. hydrarg. ammon. dil. was used; here again, unless the patient was sensitive to mercury, the preparation was too strong. The late Sir Norman Walker advised that 5 gr. of hydrarg. ammon. to the oz. should be used, and years of experience have shown me the correctness of this advice. I believe that the reason why hydrarg. ammon. has fallen into disfavour is because this advice has been neglected.

3. The ointment base for the penicillin was described as too soft. It consisted of equal parts of cod-liver oil, lanolin, and water. Might I suggest to Surg. Lieut. Gold that the next time he uses penicillin he should try 5% lanolin, 20% water, and 75% liquid paraffin if a soft cream is required, or 75% paraffin. molle if a firmer cream is wanted.

I do hope he will understand the spirit in which I make these remarks. I enjoyed his well-written article and I feel that he has done dermatology a great service, for, like the poor, impetigo is always with us, and its treatment has many angles and pitfalls.—I am, etc.,

Paignton. ARTHUR J. AMBROSE.

Artificial Insemination

SIR,—Artificial insemination of a wife by her husband's semen is a very different matter from a similar procedure in which the semen comes from another selected man or from a pool.

In every civilized community parenthood carries responsibilities for the care and upbringing of the child. It is difficult to understand how any reasonable man can in cold blood consent to take part in the procreation of children in whose upbringing he deliberately refuses to take part. Such conduct

conflicts with all civilized standards of rectitude, and would seem unwise even on grounds of expediency.—I am, etc.,

London, W.1. V. ZACHARY COPE.

SIR,—Not everyone would willingly become involved in this discussion on artificial insemination, but loyalty to the traditions and good name of medicine may sometimes transcend personal inclinations, and therefore I do not propose to let Mr. Kenneth Walker (Feb. 10, p. 199) disappear behind the smoke screen of a quotation from Voltaire. For all the relevance this has to his thesis, he might as well have ended his letter by inditing "Rule, Britannia." No one objects to his stating his ethical position; the objection is that he appears to have none. His situation is that artificial insemination by donated semen is practicable and therefore requires no other justification. What the cattle breeder does, we may do.

Let us look this business fully in the face so that all its implications may be clear. We are told that the qualifications of the human stallion, and what is asked of him, are that he shall be a married man of "intellectual attainments," between 30 and 45 years of age, and the father of two legitimate children. He should be of high fecundity, acceptable character and viability, and his "other qualifications" must meet with the august approval of the specialist in the new science of siphoseminology. He must be subjected to periodical tests of his seminal products, and should he be willing and able to deliver these to the laboratory twice weekly—presumably in a plain van—he might theoretically become the father of 400 children a week. However, his total of offspring is to be arbitrarily limited to 100, after which he retires upon his well-earned laurels. In his unsearchable wisdom the inseminator will decide which of his private stud of human stallions best meets the needs of the particular female candidate for insemination. The donor's wife finds no mention in this prospectus. Presumably the donor must keep from her the secret of his perverted philoprogenitive cravings, or he will need a wife as degraded as himself, one who, the mother of two of his children, does not object to his acting as sire to an indefinite number of human females.

One can but marvel at the grandiose frame of mind of the inseminator, who conceives himself fit to assume these superhuman prerogatives, and to people the land with a new race that shall improve upon the handiwork of Providence. In time, doubtless, we shall be presented—in due scientific form—with an analysis of the careers and achievements of these siphogens.

But this is not all. If so much is unobjectionable, the business can surely with equal freedom from reproach be carried still further. There must be unmarried women whose lives might be rounded off by maternity. Why not render this "service" available to them? Then there are thousands of married men over-seas unable to raise families. Might not these wish to give some sort of power of attorney to the inseminator, to permit his donors and his syringe to act as proxy for them? If we begin where are we to stop? Why stop, indeed, short of exploring the full possibilities of the new technique? A syringe has no ethics, and can impart no ethical sanction to a transaction of this order. Why bother about it? After all, ethics are merely a matter of "feeling," which is Mr. Kenneth Walker's naive way of saying that a little of what you fancy makes you good.

When techniques come into the irresponsible hands of the ethically rootless they are a constant threat to both intellectual and ethical values, as we may see when we gaze round us upon a world in which man is torn and tormented by the fruits of techniques he has neither the wisdom nor the sense of values to control. Medicine now is being invaded by this evil, and every thoughtful doctor who holds dear the traditions of medicine as a humane and learned profession must feel called upon to protest in unequivocal language.—I am, etc.,

London, W.1. F. M. R. WALSHE.

SIR,—While reading the other day the chapter on sterility in *Diseases of Women*, by Ten Teachers (1930 ad.), I came across the following passage relative to artificial insemination. "This method is successful sometimes with domestic animals, but is naturally somewhat repugnant to *normal* human beings, though some women resort to it in desperation." (The italics are mine.)

In a letter (not published) which I sent to you several months ago on this subject there occurred the following questions: "What sort of a woman is it who demands artificial insemination? If the maternal urge in a childless woman cannot be satisfied by the adoption of a suitable child, is she not better without one altogether?" The question is whether she is concerned about the thwarting of her own feelings of motherly love or whether it is her own sense of frustration and inferiority as compared with other women who have children which troubles her most. One suspects such women of having a neuropathic tendency, and it would be of interest to see the life history of the offspring of this method of procreation for evidence of psychoneurosis which they might inherit from the maternal side.

We have yet to have the views of the leaders of the profession in the realm of obstetrics and gynaecology as to this seemingly thorny question, which bristles with moral, if not medical, difficulties. One imagines that the stomachs of the average medical man and woman, in spite of nearly six years of war and Nazi horrors, still retain sufficient sensitivity to experience some feelings of antiperistalsis when discussing this subject.—I am, etc.,

Hove. G. L. DAVIES.

SIR,—Recent letters on the subject of artificial insemination reveal a peculiar emotional attitude in many of your correspondents. They seem to regard the operation with the same sort of horror which antivivisectionists and antivaccinationists have towards their pet aversions.

It is difficult to obtain any idea of the extent to which artificial insemination may be used, but the number of operations will undoubtedly be small, and may possibly be insignificant when compared with the number of illegitimate pregnancies, the number of illegal operations, or the number of pregnancies averted by contraception. To me the matter is one purely for the consciences of the applicants, and if a couple wish to resort to this method to obtain a child they should be allowed to do so, as the alternative would seem to be for the wife to commit adultery, which is just as illegal and unethical.—I am, etc.,

Hebburn, Co. Durham. J. A. FORREST.

Health of Children in Day Nurseries, 1944

SIR,—Referring to recent correspondence in connexion with the health of children in wartime day nurseries, the accompanying figures may be of interest. As some of the data on which diagnoses were based were somewhat vague the figures can be accepted only provisionally and regarded merely as a rough indication of the extent of illness in the Halifax wartime nurseries. So far as I can ascertain (and allowing for the difficulties and inadequacy of morbidity statistics) they compare favourably with morbidity rates for non-nursery children in this area.—I am, etc.,

Nursery Index	Average Monthly Attendance		Measles and/or Rubella	Whooping-cough	Diphtheria	Scarlet Fever	Bronchitis	Pneumonia	Pulm. T.B.
	0–2 yrs.	2–5 yrs.							
L.B.	14	Nil	10	6	Nil	Nil	3	2	Nil
B.H.	17	Nil	15	Nil	Nil	Nil	2	2	Nil
C.L.	13	21	6	7	Nil	1	2	1	Nil

G. C. F. ROE,
Medical Officer of Health,
Halifax County Borough.

Psychology's Opportunity

SIR,—It seems a pity that the *Journal* should, through an editorial note to a letter from one of its correspondents (Feb. 3, p. 164), ascribe (even though only partially and by implication) the great successes of the Red Army to an "aggressive instinct" traditional to our Allies. The manner in which they have endured hardships appalling to contemplate and yet have preserved their ability to stage colossal victories has been ascribed to an infinite capacity for suffering, a docile patience, an animal-like willingness to accept discipline imposed from above, a reckless disregard for human sacrifice, and other qualities supposedly traditional to the Russian peasant or to the "Slav" temperament. That any degree of credence should be given

to such an unscientific view in a reputedly scientific journal is regrettable. It would appear that Red Army men are themselves getting rather tired of this explanation for their deeds of prowess. An article in a recent issue of *Red Star* (the newspaper of the Red Army) says:

"It is time to see us for what we are—to study us, not from old fables and legends, or even from Dostoyevsky, but from a current textbook—our present-day deeds and our living people. . . . Foreigners are astonished at our victories. The world must have been asleep. It failed to see that we were learning to write, to build, and to fight. We are winning to-day not because our Cossacks are dashing, or because of the infinite docility of the old Russian soldier. The Red Army man knows why he is fighting and for what. And if certain foreign wiseacres know that the Red Army is winning thanks to the traditional qualities of the Russian soldier, we are entitled to retort: 'You praise Platon Karatayev only because you don't like the October Revolution.'"

The Russians evidently attribute their victories to their socialist way of life. They, of all people, should know.—I am, etc.,

Cymla, Neath. T. FRANCIS JARMAN.

SIR,—With all deference may I point out that your note under Dr. Tandy Cannon's admirable letter (Feb. 3, p. 163) in no wise weakens, much less nullifies, the truth of the latter's thesis, your note being in the nature of an *argumentum ad hominem*. The "aggressive instinct" of the Russians in its present manifestation is comparable to the surgeon's knife when used (granted without an anaesthetic) to extirpate a cancer threatening the welfare, and indeed the life, of every nation, including that of Germany itself.—I am, etc.,

Royal Societies Club, London. GEORGE S. BROCK.

Demobilization and the E.M.S.

SIR,—I feel that the letter of "E.M.S." (*Journal*, Jan. 20, p. 97) calls for further comment. Certainly the majority of Service M.O.s do not spend more than a small proportion of their time sitting beside a slit trench; nevertheless, they have sustained a considerably higher mortality and morbidity than E.M.S. officers. This, however, is beside the point, and in actual fact the tedium of uneventful patrols at sea is often harder to bear than the dangers of enemy action. The essential point is that while "E.M.S." has continued to do professional work and to increase his post-war market value by the acquisition of a diploma in anaesthetics, we in the Services have lost through disuse much of our skill and gained little beyond a well-found cynicism.

"E.M.S." speaks of the compensations of Service medicine with little sense of reality; the rank of lieutenant after five years loses its glamour, while the promised gratuity will not pay for the re-education we shall require.

Mutual recriminations, of course, are entirely profitless, but one solution does present itself. The release of E.M.S. officers for the Services would allow them to have their share of travel and prestige; while Service M.O.s (who might, after all, have escaped the London "blitz" because they were in Crete or Tobruk) would gladly take their place in the E.M.S. Incidentally it might interest "E.M.S." to know that "blitzed" homes are not confined to civilian doctors. I also have had my wife and child bombed out.—I am, etc.,

"R.N.V.R."

Service Medicine

SIR,—As a chemist whose children are both budding "medicals," I have followed with interest the recent correspondence in the *Journal* about Service medicine. So, apparently, has my son, now serving with a specialist R.A.M.C. unit over-seas, where he has come into contact with a large number of medical officers of all types. Because he has thus had a good opportunity of gauging the opinion of the younger medical officers, and has written to me quite frankly what he thinks on this subject, with no notion whatever of publication, you may think it useful to reproduce the relevant part of his letter which I give below, with only such slight elisions as are necessary to preserve anonymity.

"There has been a lot of mud-slinging in the *B.M.J.* recently. Several (obviously junior) officers have written letters, hiding behind screens like 'Temporary Serving Officer.' They have all said that Service medicine was a very poor show because they didn't see enough sick men, and because promotion was too much on the 'old chap' basis and not on the 'clever boy' basis. More senior officers than I had realized to exist in the Medical Services have haughtily stood their ground in the face of this mutiny. What they say is roughly: (1) Patients are better treated in the Army than in civil life (I agree about this). (2) Doctors in the Army must administrate as well as ministrate. (I'm afraid this is too true.) (3) The cowardly chaps who write these letters anonymously are in a minority. Most M.O.s love the dear old Army. They seem sure about this. I am equally sure that most junior medical officers in the various Services feel they would prefer to have a job in a civilian hospital. The only way these scribes are in a minority is that they think it will do any good to write letters about it. Most M.O.s just manage to be cheerful and to do what little work is offered to them. Mostly they feel it is in bad taste to complain about their lot when men skilled at other jobs have an even more unprofitable time in the Army, as well as a more dangerous time. Mostly they lapse into a shock-absorbing state of relaxation about the whole business.

In the Army there are two different kinds of medical officer: (1) There are middle-aged men hoiked out of their lucrative general practices to try and pay their life insurance premiums on a captain's pittance—as it seems to them. They rather resent the fact that they are pushed around by adolescent young puppies with the rank of major or colonel. And it's much rougher, I suspect, to be uprooted at the age of 40 than it is at the age of 30. So the middle-aged G.D.O.s (general duty officers) are the hardest-treated ones. (2) There are newly qualified chaps being paid what they regard as a prince's salary for doing less work than they ever did before. Like everyone nowadays they want to be specialists, but they hadn't been qualified long enough in civil life to realize that they would have to be G.P.s. As time passes they are coming to see it anyway, and they blame it on the Army. These are the ones most of whom *don't* write letters to the *B.M.J.*

But the brigadiers writing letters in the *B.M.J.* are wrong if they imagine that most medical officers really like the Army. The more cheerful ones try to cheer up the gloomier ones by pointing out its brighter side. And, of course, anyone speaking to a brigadier tries to give the impression that he's a happy and contented sort of bloke, but when Major X and I, in our travels, met a medical officer who did really prefer the Army to civil medicine we drew back from him as we would from someone who announced, 'I'm Napoleon.' If there had been a brigadier in the room his behaviour might have been understood, but there wasn't. Anyway, one of the good things about the Army is that most brigadiers are human, and don't particularly like being Army doctors themselves, though they quite enjoy being brigadiers."

—I am, etc., UNIVERSITY TEACHER.

WAR INJURIES

EXHIBITION OF SPECIMENS

After the destruction by enemy action in 1941 of the Army Medical War Collection housed in the Museum of the Royal College of Surgeons, London, the Medical Research Council accepted a request from the War Office and the Royal College of Surgeons of England that they should assist with arrangements for forming a comprehensive national collection of pathological specimens, photographs, and drawings of war injuries, which would serve both for teaching purposes and as a permanent record of the types of injury sustained in the present conflict. A special subcommittee of the Council's War Wounds Committee was appointed to direct the scheme; this subcommittee includes nominees of the three Services, the Ministry of Health, the Department of Health for Scotland, the Royal College of Physicians of London, the Royal College of Surgeons of England, and the Ministry of Pensions. The arrangements for the collection were entrusted to Dr. Joan M. Ross, who is acting as temporary curator.

A large number of specimens have now been accumulated, and by kind permission of the Royal Society of Medicine an exhibition of a selection of these is to be held in the Society's Council Room from March 5 till March 9, both days inclusive, from 9 a.m. until 6 p.m. The exhibition will be open to all members of the medical profession, but not to the general public. The exhibition will consist mainly of specimens, photographs, and drawings of wounds sustained in the land fighting in Italy and North-West Europe, which have been collected with the co-operation of the Army Medical Department. It will include museum specimens, collected by Dr. Ross; coloured photographs by Mr. P. G. Hennell (by courtesy of the Metal Box Co., Ltd.); drawings by Mrs. M. L. Wright and Mrs. Ehrenborg. It is hoped that all medical men or women having specimens of relevant interest to offer to the national collection will communicate with Dr. Ross, Science Block, Mill Hill School, London, N.W.7 (Mill Hill 3640). It is intended that the specimens collected shall be distributed to appropriate museums and teaching institutions after the war.

Obituary

E. A. PETERS, M.D., F.R.C.S.

Mr. Edwin Arthur Peters, consulting surgeon to the nose, throat, and ear department of University College Hospital and to the Bolingbroke and Paddington Green Children's Hospitals, died in London on Jan. 29.

He took a first-class in the Natural Sciences Tripos at Cambridge and the M.D. degree in 1900. In 1903 he took the F.R.C.S.Eng. He soon decided to devote himself to ear, nose, and throat practice, and was appointed to the staff of the Royal Ear Hospital, which was subsequently amalgamated with University College Hospital, and later to the Bolingbroke and Paddington Green Children's Hospitals. He was an active member of the Laryngological and Otological Sections of the Royal Society of Medicine and occupied the presidential chair in the latter. During the last war he became a captain, R.A.M.C., and was in charge of the nose, throat, and ear department of the Royal Victoria Hospital, Netley.

Mr. Peters's main literary contribution was his association with Richard Lake in the later editions of the well-known manual *Diseases of the Ear*, but he also contributed a number of articles on the special subjects in various journals. During his younger days he carried out investigations on the distribution of the peripheral nerves and the bacteriology of diphtheria. With the late Dennis Embleton he collaborated in an inquiry into the relation of sphenoidal sinus infections with cerebrospinal meningitis. He was intensely interested in the clinical side of his subjects and was a most regular attendant in his hospital departments. He always welcomed the visit of a colleague, and willingly gave of his knowledge in solving difficult problems.

In private life he had many hobbies—yachting, shooting, and carpentry among others—and he was devoted to country life. He was married twice, first to Alice Serjeant, by whom he had two daughters, one of whom is the well-known industrial dermatologist and the other an artist of distinction. Later he married Margaret Mains, by whom he leaves two children, a boy and a girl.

The medical profession has suffered a great loss by the untimely death at the age of 39 of HUGH CARMALT. He was in practice in Birmingham until August, 1939, when he joined his Territorial battalion. He served over-seas until the Dunkirk evacuation, and was awarded the *M.C.* for the part he played in this. It was in the intensive training period that followed Dunkirk that his fatal disability was caused—a chafing gaiter on the march, a phlebitis, a coronary thrombosis, and permanent invalidism. His outstanding quality of courage which had been recognized by his military award was now evident to all who came in contact with him. The struggle against his affliction won the admiration of a large circle of medical and non-medical friends. He tried to return to general practice, was seriously ill again, recovered a measure of his former health, and determined to break new ground. He entered upon a course of studies at Moorfields, and in July of last year successfully completed the first part of the D.O.M.S. examination. Within a fortnight of the date on which he had entered to sit for the final part of the D.O.M.S. his long illness had a sudden fatal termination. Hugh Carmalt had a great gift of patience which endeared him to many hundreds of patients before the war and stood him in good stead in the last uneasy months of his life. He leaves a widow and two young children.—L. H. G. M.

Dr. ROBERT FENNER died in retirement on Dec. 10 at Liphook aged 85, having continued in active practice up to the age of 80. He qualified at the age of 21 from King's College Hospital, where as a student he had been dresser to Lord Lister, and spent a couple of years after qualification as medical officer to the copper mines at Betts Cove and Tilt Cove, Newfoundland. His work there gained him the Fellowship of the Royal Geographical Society. He practised for many years at Cromer, where he attended numerous well-known people, including the late Emperor of Austria and King Edward VII. He moved to London in 1897 and worked for many years more in partnership with the late Sir M. Abbot-Anderson, and in 1898 he accompanied Kaiser Wilhelm II and his Empress on their tour to Palestine. He was well known at the Royal Thames Yacht Club and at one time owned the yacht *Chough*. During the last war he was chief constable of the Marylebone Police Volunteers and head of the Thames Police Patrol. That war brought him cruel losses, for his two sons were killed in 1917 and 1918, one in the Scots Guards and the other in the Navy, and his daughter also died, but he found some consolation afterwards in a particularly happy second marriage late in life. Fenner was a man of handsome appearance, combined with a most courteous manner and kindly disposition, and it is not surprising that he retained the confidence of so many distinguished patients. The outbreak of the present war compelled him to leave London at the end of 1939, and he had outlived many of his friends, but those who remain will remember his striking figure and, above all, his kindness and loyalty. They will be glad to know that he retained his vigorous personality to the end and died quickly from a cardiac attack, with little suffering.

Dr. GEORGE SHEPHERD WILSON, for 12 years medical superintendent of the Durham County Mental Hospital, Winterton, Sedgefield, Stockton-on-Tees, died on Jan. 31 at the age of 47. He was a native of Greenock and was educated at Glasgow University, where he graduated M.B., Ch.B. in 1921. He saw service in the war of 1914–18 and was invalided out of the Army as a result of becoming a gas casualty. After graduation he acted as house-surgeon in the Glasgow Western Infirmary, and from there went to the Lancashire County Mental Hospital at Prestwich. He obtained his D.P.M. in 1929 and relinquished the post of first assistant at Prestwich to become medical superintendent of the hospital at Winterton. His twelve years in the County of Durham were indeed fruitful, and it was due to his energy and vision that the present modern units—reception and administrative—took shape and expression. He promoted and directed the establishment of psychological clinics at Darlington and Durham City, and he was ever eager to apply the most modern methods to the treatment of the mentally afflicted. The outbreak of war added fresh burdens to an already crowded life, and it fell to his lot to found and to guide the Emergency Medical Services Hospital, which many will remember with pride and gratitude. Despite all demands upon his strength and attention he never failed to give of his best.

ROBERT BLAIR KINLOCH, M.B.Lond., who had been in general practice in St. Albans since 1904, died on Feb. 5 at St. Bartholomew's Hospital at St. Albans after a very brief illness, at the age of 69. He was born in Cardiff in 1875, and crowned his career at St. Thomas's Hospital by winning the Mead Medal. A correspondent writes: Dr. Kinloch was unsurpassed in St. Albans as an obstetrician, and few were his equals as an anaesthetist. He was truly a family doctor, for he devoted himself to his patients, and they in turn were devoted to him. His work was his life, and his patients loved him for his unfailing kindness and gentleness, so that he became not only their doctor but their guide and counsellor and trusted confidant, for his advice was sought on all manner of subjects. He would never commit himself to an answer until he had turned the matter over in his mind for some time, thus ensuring that his answer, when given, carried the full weight of his mature thought. In the first world war he served in France, and was for a time at Ostrahove Camp at Boulogne. His second son, Robert Alastair Boys Kinloch, M.B., captain, R.A.M.C., was killed in Burma in May, 1944, while acting as R.M.O. to the 1st Btn. King's Regiment. This tragic news, coupled with strain from overwork (for he never spared himself) and a serious collapse early in 1941, was undoubtedly a contributory cause of Dr. Kinloch's death.

The Services

The appointment of Surgeon Vice-Admiral Sir Sheldon Dudley, K.C.B., M.D., F.R.C.P., F.R.S., as Medical Director-General of the Navy has been extended for a further six months from July 2, 1945.

Col. N. C. Speight, N.Z.M.F., has been appointed C.B.E. (Military Division), and Brig. J. M. Twhigg, D.S.O., N.Z.M.F., has been mentioned in dispatches, in recognition of gallant and distinguished services in the South Pacific during the period Feb. 1 to July 31, 1944.

The King of Egypt has conferred the Insignia of the Third Class of the Order of the Nile on Lieut.-Col. A. G. Harsant, O.B.E., R.A.M.C., on the occasion of his retirement as professor of clinical surgery in the Faculty of Medicine at Fouad University.

Surg. Lieut. E. J. Gilmore, R.I.N.V.R., has been commended for good services in fire-fighting after an explosion at Bombay Docks.

CASUALTIES IN THE MEDICAL SERVICES

Officially reported died of wounds.—Capt. Reidar Scott Holtan, R.A.M.C.

Medical Notes in Parliament

Increased Grants to Universities and Medical Schools

On Feb. 13 Mr. SALT and Sir E. GRAHAM-LITTLE asked the Chancellor of the Exchequer whether he was now in a position to make a statement on the provision to be made to meet the post-war requirements of the universities. Sir JOHN ANDERSON replied: I have carefully considered the report made to me by the University Grants Committee on the probable financial needs of the universities in Great Britain during the first decade after the war, and I have also had the advantage of hearing the views of a deputation of representatives of the universities and university colleges. It is clear that if the universities are to play the part they should in the reconstruction of our national life after the war they will have to incur expenditure on a very much higher scale than before the war. It is also clear that if the future financial needs of the universities are to be met, a large share of this new expenditure will have to be met by the Exchequer. As regards recurrent expenditure, it is not easy to forecast with any accuracy what will be the actual expenditure of the universities during the transitional period between war and peace. Both the University Grants Committee and the universities themselves have emphasized the importance of not sacrificing quality to quantity, and it follows that in the immediate future the supply of adequately qualified staff will be a limiting factor on development. The increased expenditure to be incurred by the universities will not, therefore, be spread equally over the 10-years period of the Committee's review. It will be heavier during the later than the earlier years of the decade, and the Government recognizes that the grants to universities during those later years will need to be further and substantially increased above the level now proposed for the next two years.

The University Grants Committee has recommended that the present annual vote for the universities of £2,149,000 should be increased for each of the next two financial years by the addition of £2,000,000 for general university purposes, £1,000,000 for developments in the medical schools arising out of the recommendations of the Interdepartmental Committee on Medical Schools, and £500,000 for grants for teaching hospitals as recommended by that committee. The Government has decided to accept the recommendations of the University Grants Committee for the two years in question. The question of the grant for future years will need to be reviewed at the end of the two years.

With regard to expenditure for capital purposes, the needs of the universities have in the past been met for the most part by private benefactions. I am advised by the University Grants Committee and the universities that this source of support cannot be expected to meet the needs of the universities for capital developments in the years following the war, and that if the building programmes of the universities are to be carried out a large share of the cost will have to be met from the Exchequer. The University Grants Committee has estimated that the universities will need to expend about £18,750,000, calculated at pre-war prices, on capital developments during the decade, and the Interdepartmental Committee on Medical Schools estimated that an additional sum of £10,000,000 (also at pre-war prices) will be required for developments in the medical schools. The Government accepts these estimates as indications of the probable scale of necessary capital developments, and recognizes that a very substantial proportion of the money will have to be provided from the Exchequer.

In view of the restrictions on buildings which are likely to operate during the years immediately after the war, it seems unlikely that the universities will have opportunities for any considerable capital expenditure during the next year or two. In the circumstances it seems to me that it will be sufficient to include in the Estimates for the coming year a token sum of £250,000 for distribution by the University Grants Committee, without prejudice to what may be necessary in later years. Accordingly, I am including in the 1945 Estimates £5,900,000 as a grant-in-aid of universities, colleges, medical schools, and teaching hospitals (Great Britain). It should not be assumed, however, that this amount will need to be distributed in grant within the financial year. This matter will be within the discretion of the University Grants Committee, which will review the position from time to time in the light of developments and may elect to retain part of the provision in the deposit account into which the grant-in-aid will, as usual, be paid. Any amount so retained will not in any case be liable to surrender to the Exchequer at the end of the year, but will remain available for distribution in the future.

Replying to questions, Sir John Anderson said that in the event of the £250,000, which was really not much more than a token sum, proving insufficient, the possibility of its being increased within the financial year would certainly not be ruled out. Dr. SUMMERSKILL asked what period of grace the Chancellor proposed to give those medical schools which now only admitted men to allow them to make arrangements for the admission of women before he withheld grants in those cases where they refused to do that. Sir JOHN ANDERSON: I am glad to say that that particular question has not so far come within my jurisdiction.

Diphtheria in Lincolnshire

Asked on Feb. 8 by Mr. Viant how many cases of diphtheria had been notified in the three divisions of Lincolnshire since 1939, and how many deaths from that disease had been recorded in those areas, Mr. WILLINK provided the following table:

	Holland (A.C.)		Kesteven (A.C.)		Lindsey (A.C. and Associated C.B.s)	
	Notns.	Deaths	Notns.	Deaths	Notns.	Deaths
1940 ..	54	3	85	4	339	12
1941 ..	61	4	50	4	323	18
1942 ..	72	2	32	2	383	11
1943 ..	19	0	22	4	397	16
1944 (1st 3 quarters)	13 (a) 6 (b)		12 (a) 12 (b)		239 (a) 216 (b)	

Notes

1. All the notifications and deaths refer to civilians only.
2. The notifications for the years 1940–3 allow for such partial corrections of original notifications as were supplied to the Registrar-General.
3. For 1944 notifications are for the first three quarters of the year and no figures for deaths are yet available: (a) represents the numbers originally notified and (b) the numbers as finally corrected.

Protective Power of Vaccination

On Feb. 14 Sir JAMES GRIGG, replying to Mr. Leach, said it had never been claimed that vaccination conferred 100% immunity against smallpox in all cases and under all conditions. The maximum degree of immunity was estimated to develop about 14 days after vaccination; thereafter it gradually waned, but it remained effective, under normal conditions, for five years in the United Kingdom and for three years in Egypt, where the risk of infection was somewhat greater. During an epidemic, whenever it occurred, the virulence of the infecting agent was such that even the maximum degree of immunity conferred by immediate revaccination was not in every individual case sufficient to resist the disease. Nevertheless, experience had shown that the revaccination of all exposed to infection, coupled with the normal precautions of immediate isolation of infected persons and restriction of movement of possible "contacts," was successful in giving immunity to all but a small proportion and in quelling an epidemic.

Universities and Colleges

UNIVERSITY OF OXFORD

Somerville College announces that Miss Helen Darbishire will be succeeded as Principal of the College by Dr. Janet M. Vaughan, F.R.C.P. Dr. Vaughan is medical officer in charge of the North-West London Blood Supply Depot for the Medical Research Council. She was an undergraduate of Somerville College and took a first class in physiology in 1922 and her D.M. in 1930. She has been a Rockefeller Fellow, a Beit Memorial Fellow, and a Leverhulme Fellow, has held the post of assistant clinical pathologist at University College Hospital and the British Postgraduate Medical School. Her book, *The Anaemias*, is in its second edition. She was a member of the Interdepartmental Committee on Medical Schools (the Goodenough Committee), and is now a member of the Royal Commission on Equal Pay and of the body appointed by the Government to investigate public health in India.

UNIVERSITY OF CAMBRIDGE

At a Congregation held on March 2 the following medical and surgical degrees were conferred:

M.D.—R. I. N. Greaves.

M.B., B.CHIR.—(All by proxy) C. D. Drew, H. H. E. Batten, D. W. R. Lyle, I. A. Magnus, T. J. S. Patterson, A. N. Pearson.

Medical News

A general meeting of the Medical Society for the Study of Venereal Diseases will be held at 11, Chandos Street, W., to-day (Saturday, Feb. 24) at 2.30 p.m., to consider the proposals of the committee of the society on "The General Principles of Administration and Staffing of the V.D. Clinics." The discussion will be opened by Dr. I. N. Orpwood Price.

The Royal Sanitary Institute has postponed the sessional meeting to have been held in Liverpool to-day (Feb. 24).

Dr. H. B. Morgan, M.P., medical adviser to the Trades Union Congress, will deliver an address on "Health and Industry" to a meeting of the Polish Medical Association in the United Kingdom on Tuesday, Feb. 27, at 5 p.m. in the Hastings Hall of B.M.A. House. All who are interested will be welcome.

The following films will be shown by the Scientific Film Association at the Royal Society of Medicine, 1, Wimpole Street, W., on Wednesday, Feb. 28, at 5.30 and again at 8 p.m.: "Mass Radiography," "Motion Pictures of the Larynx," "Liver Fluke," "Accident Service." Admission will be by ticket only, and application should be made immediately to the honorary secretary of the Medical Committee, Dr. S. J. Reynolds, 14, Hopton Road, London, S.W.16.

A meeting of the Council of the Medical Superintendents' Society will be held at Queen's (L.M.S.) Hotel, Birmingham, on Saturday, March 3, at 10 a.m., and will be continued on March 4 if necessary.

Sir Henry Dale, P.R.S., will deliver three lectures on "Nerve-endings and Chemical Transmitters" before the Royal Institution, 21, Albemarle Street, W., on Tuesdays, March 6, 13, and 20, at 5.15 p.m.

The annual general meeting of the Society of Public Analysts and Other Analytical Chemists will be held at the Chemical Society's Rooms, Burlington House, Piccadilly, W., on Friday, March 9, at 3.15 p.m., and will be followed by the presidential address by Mr. S. Ernest Melling on "Water and Water Supplies."

The annual general meeting of the Institute of Hospital Almoners will be held at Caxton Hall, Westminster, S.W., on Friday, March 9, at 5.30 p.m., when Sir William Beveridge will give an address.

Prof. David Brunt, Sc.D., F.R.S., will deliver an address on "Climate and Human Comfort" before the Royal Institution, 21, Albemarle Street, W., on Friday, March 9, at 5 p.m.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* there were 3,098 more cases of measles than in the previous week, and 81 more of dysentery. Whooping-cough, scarlet fever, and diphtheria, on the other hand, dropped in incidence—by 123, 109, and 35 cases respectively.

Diphtheria notifications fell most markedly in the north. Local notifications of whooping-cough fluctuated, and the only large variation was a fall of 59 in Lancashire. The incidence of measles rose sharply in most areas, increases being recorded as follows:—Yorks West Riding 880, Surrey 314, Middlesex 251, London 192, Yorks East Riding 152, Durham 127, Cumberland 116, Lincolnshire 103, Lancashire 103; the only decline of any size was in Warwickshire, where 169 fewer cases were recorded.

There were two fresh outbreaks of dysentery during the week: 32 cases were recorded in Cambridge M.B., and 22 in Bath C.B.; 56 cases were reported from the outbreak in Buckinghamshire, Aylesbury R.D. Other large returns were London 45, Essex 43 (Southend-on-Sea C.B. 35), Yorks West Riding 27, Lancashire 26, Gloucestershire 20, Northumberland 15, Middlesex 13.

In *Scotland* the measles incidence fell by 80, diphtheria by 39, and scarlet fever by 19. Diphtheria notifications were at the lowest level in recent months. There were 25 more cases of dysentery than last week; the chief outbreaks were Glasgow 26, Stirling 23, Edinburgh 11, Lanark County 11.

In *Eire* notifications of diphtheria fell for the fourth consecutive week, and the 83 cases marked the lowest total of recent months. An outbreak in Dublin, Clifden R.D. 16, accounted for the rise in the incidence of measles.

In *Northern Ireland* notifications of measles continued to drop; during the past five weeks the weekly total has fallen from 281 to 139. A small rise in scarlet fever, 13, was reported for the fourth week.

Week Ending February 10

The returns of infectious diseases in England and Wales during the week included: scarlet fever 1,466, whooping-cough 1,516, diphtheria 402, measles 20,627, acute pneumonia 1,449, cerebrospinal fever 94, dysentery 324, paratyphoid 2, typhoid 6. Influenza was responsible for 67 deaths in the great towns.

No. 5

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Feb. 3.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (*b*) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1945 (a)	(b)	(c)	(d)	(e)	1944 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	76	7	26	9	3	71	4	23	4	—
Deaths		3	—				—	2		
Diphtheria	415	18	112	83	10	733	35	187	145	26
Deaths	4	—	2	1	1	15	2	2	6	—
Dysentery	376	45	104	—	3	161	18	97	1	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	3	—	1	1	—
Deaths		1					—			
Erysipelas			56	6	2			32	10	1
Deaths		1					—			
Infective enteritis or diarrhoea under 2 years				16					10	
Deaths	66	4	8	11	3	47	12	9	20	3
Measles*	16,039	573	478	34	139	1,162	206	113	241	1
Deaths	11	—	7	—	1	—	—	—	1	—
Ophthalmia neonatorum	67	3	19	1	—	70	5	19	1	1
Deaths										
Paratyphoid fever	2	—	—	—	—	9	1	1 (B)	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal†	1,366	90	14	23	11	1,115	69	27	4	3
Deaths (from influenza)	89	8	3	—	2	78	15	3	3	2
Pneumonia, primary			287	32				293	21	
Deaths		76		26	23		51		14	9
Polio-encephalitis, acute	1	—				1	—			
Deaths		—					—			
Poliomyelitis, acute	5	—	—	—	1	7	—	—	—	1
Deaths		—					—			
Puerperal fever		1	20		—		11	13		—
Deaths										
Puerperal pyrexia‡	130	8	12	—	—	185	5	10	—	1
Deaths		—					1			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,401	37	163	21	61	2,032	147	241	36	91
Deaths	—	—	—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	4	1	1	4	—	5	—	2	5	2
Deaths	—	—	—	—	—	1	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,502	65	110	41	17	2,116	172	143	66	22
Deaths	13	3	4	2	—	13	1	1	3	1
Deaths (0–1 year)	609	56	61	68	34	438	58	74	59	20
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	8,032	1105	979	389	217	4,981	799	669	246	144
Annual death rate (per 1,000 persons living)			22·2	25·1	§			15·4	16·1	§
Live births	6,595	722	828	414	230	6,638	813	877	415	282
Annual rate per 1,000 persons living			16·6	26·7	§			17·8	27·1	§
Stillbirths	199	14	32			240	37	39		
Rate per 1,000 total births (including stillborn)			37					43		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

§ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

Letters, Notes, and Answers

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ANY QUESTIONS?

Hallucinations in Old Age

Q.—*A woman aged 78, with excellent mental and physical family history, has of late developed hallucinations at night time. Men or women or animals appear when ? awake, and when she rises to accost them or drive them away they vanish. Is this a serious condition? By day she is quite well, but has B.P. of 200/96.*

A.—Hallucinations, particularly visual ones, and especially when occurring in a dim light, are an indication of a slight confusional state. In this case this could be adequately accounted for by age and presumable consequent slight organic changes in the brain. But it might also be due to a toxic effect. If bromides are being taken, they would be better omitted and replaced by another sedative; sodium chloride should then be given to displace the bromide from the blood. Otherwise it might be worth trying fairly heavy dosage with nicotinic acid. If neither of these causes is operating, the hallucinations can be attributed to vascular changes, but the prognosis for life and sanity is not much affected. Some deterioration can be expected fairly soon in any case.

Choice of Contraceptive

Q.—*What is the best contraceptive for a woman in the forties who has had two children and has no indications of the onset of the menopause? If you advocate a cervical cap and concurrent use of a chemical contraceptive, would you also give some advice on the fitting and hygienic use of such a contraceptive method? Are the cervical caps supplied in various sizes, as the fit of such a pessary must be an important factor in the success of the method? What length of time should elapse after intercourse before it is safe to remove the cap, and should a vaginal douche be used at the same time?*

A.—In this case, as in any other, the method of choice of contraception will depend upon the degree of security required and the preference of both partners. It is wisest to consider a woman as potentially fertile until a year after her last menstrual period. If a third pregnancy would be no disaster, the use of a contraceptive suppository could be advised. If a high degree of security is requested, either the husband must use a condom or the wife must be taught to use an occlusive cap of some suitable kind—a "cervical" type is actually the one least preferred by experts. It would be beyond the scope of this answer to describe the technique of fitting, and teaching the use of, occlusive caps: this technique, like, say, the choice of ocular lenses, requires tuition and experience. Reference will be found in textbooks, or in Butterworth's *British Encyclopaedia of Medical Practice*. Most authorities instruct a woman to cover the occlusive cap with a spermicidal ointment, and if it is not removed until 8 or 10 hours have passed no douche is necessary, for the spermatozoön cannot survive so long in the vaginal medium.

Sulphanilamide for Burns

Q.—*In what form is sulphanilamide best used as routine treatment for burns in a factory practice?*

A.—In the form of a 3% cream made up with lanette wax, castor oil, and water, as described in the M.R.C. Special Report Series No. 249—*Studies of Burns and Scalds* (2nd paper).

Vitamin D and U.V.L.

Q.—*In certain selected cases of undernourishment, where some additional treatment is obviously indicated, would ultra-violet therapy be desirable in addition to giving vitamin D by mouth?*

A.—The antirachitic properties of the appropriate ultra-violet radiation (2,800 to 3,100 A.U.) are easily demonstrated in both animals and human beings. That their action results from the conversion of ergosterol into vitamin D on absorption can be shown by experiments *in vitro* and *in vivo*. Whether irradiation of the skin by a more extensive light spectrum is more beneficial than the ingestion of vitamin D is not easy to determine. It may, however, be stated that, in the experience of those in charge of departments where light is administered, a large proportion of children who have previously been taking vitamins in adequate dosages, but without striking result, undoubtedly derive benefit from irradiation. Even though no scientific proof is forthcoming to support it, the existence of some additional action of ultra-violet rays on the skin over and above the vitamin D production might be postulated. Although there appears to be no justification for the use of ultra-violet radiation in the absence of indications, or where vitamins by the mouth are having the desired effect, there is no reason why ultra-violet rays should be withheld where vitamins by mouth fail.

Mechanism of Fever

Q.—*Why does the temperature rise in a fever, and why does it stay up? What is the precise physiological explanation of that sudden "gearing up" by several degrees of the heat-regulating mechanism; and why, in the crisis of pneumonia, for instance, should the normal functions of the skin be so dramatically restored?*

A.—In fever due to infection the body's thermostat is set at a higher level, mainly as a result of a raised threshold for heat loss. This is believed to be the result of the action of bacterial toxins on the heat centre or centres; but the reaction is a purposive one, as the biological activities of the tissues are increased by the rise in temperature, whereas the conditions are less favourable for some of the pathogenic micro-organisms. The activity of the leucocytes is increased and antibody production is stimulated. This hypothesis has led to the use of artificial fever in the treatment of a variety of diseases, such as rheumatoid arthritis, subacute bacterial endocarditis, resistant gonorrhoea, and syphilis of the nervous system. The crisis in pneumonia occurs shortly after the appearance in the serum of a positive agglutination reaction for the pneumococcus responsible for the infection, and it is probable, therefore, that a critical fall of temperature is generally due to the neutralization of toxins and the sudden lowering of the threshold for heat loss.

Pain from Crystal Violet

Q.—*In the treatment of an indolent varicose ulcer I have applied once a day a 2% aqueous solution of crystal violet. The patient complains of extreme pain after each application. Is this painful reaction usual?*

A.—Some patients complain of pain when dyes are painted on a raw surface, and in the example quoted, since the reaction is severe, an alternative method of treatment might be considered.

Loa loa Infection

Q.—*Some cases of Loa loa infestation have appeared in Palestine, probably imported by Congo native troops. Mountjoy Elliot considers phenothiazine efficient against Filaria medinensis (Dracunculus). Has phenothiazine been used in cases of Loa loa and with what success? I would also welcome information on the toxic effects of phenothiazine.*

A.—Loiasis is common in the coastal regions of West Africa. No drug in therapeutic dosage has been shown to have any lethal action on the adult worms, which wander more particularly in the subcutaneous tissues. The microfilariae do no harm to the individual, and circulate in the peripheral blood solely for the purpose of infecting the insect host. Their removal, even if procurable by drug therapy, can therefore be only temporary and without benefit to the host unless the adult female worms from which they continuously derive are destroyed. Mechanical removal of these adult female worms when visible, as under the conjunctiva, is the only means so far known satisfactorily to achieve this end. Mechanical removal by gentle intermittent traction, with aseptic precautions, is also the most satisfactory and safe method of getting rid of *Dracunculus*.

Phenothiazine has caused a grave and even fatal haemolytic anaemia in children and is to be regarded as a drug potentially dangerous to man.

Blood-volume Estimation

Q.—*What advantages has the improved Evans-blue method of blood-volume estimation over the older methods employing vital red or Congo red?*

A.—The Evans blue (T. 1824) dye has the following advantages over the older dyes used: (1) The tedious corrections for traces of haemolysis in test or control plasma necessary for red dyes can be eliminated. (2) The dye is very stable and is somewhat less toxic. (3) The dye disappears from the blood stream more slowly. The technique recommended is that of Harington *et al.* (*Clin. Sci.*, 1940, 4, 311), where the dye is extracted into butyl alcohol and thus freed from plasma pigments and opacity.

Disappearance of Keloids

Q.—I have recently observed the disappearance of post-operative large abdominal keloids in patients suffering from deep jaundice. Have bile acids or salts ever been used as a local application for the removal of keloid?

A.—No record of an effect of jaundice or bile derivatives on keloids has been noted, but it is known that these lesions sometimes disappear spontaneously.

Bilateral Vasoligature

Q.—A woman has been told that she must not have any more children for at least five years. The usual methods of contraception have proved distasteful, and the husband inquires if he can undergo any operation to make this possible. Is bilateral vasoligation applicable in this case, and does it interfere with normal sexual relations? Is there any other suitable method?

A.—The operation of bilateral vasoligature is a simple one which inflicts no hardship on a husband and does not disturb the sexual relationship. The only difficulty likely to be encountered is in finding a surgeon to do it. As the law stands, sterilization is an illegal operation. Most surgeons would consider the advice that the wife should not have a child for at least five years an insufficient reason for carrying out vasoligature. They would say that modern methods of birth control are sufficiently effective to make them the right treatment in such a case.

Repeated Miscarriage

Q.—A woman miscarried at 3 months on two occasions. Five months after the second miscarriage she consulted me with a history of painless haemorrhage after 10 days' amenorrhoea. On examination the os was tightly closed, the uterus normal in size, but there was a small mass in the right fornix, suspected to be an ectopic gestation. No pregnancy was found on operation, but the right tube was much thickened and bound down with adhesions, probably from a chronic appendix removed in 1937. Both ovaries contained over a dozen retention cysts, each about the size of a pea. The tube was freed, the cysts ruptured, and the abdomen closed. The patient wants to have a baby. What is the cause of the non-rupture of the follicles, and is the prognosis for a future pregnancy good or bad? Is treatment with gonadotrophic hormone of the pituitary of any use in these cases?

A.—Cystic ovaries of this type are not uncommon and do not necessarily have any pathological significance, but from the description it is not easy to decide the nature of the cysts in this case. The cysts were probably atretic follicles, but since the menstrual cycle was disturbed it seems likely that one or more of them contained functional granulosa or lutein tissue. The presence of numerous small cysts does not inevitably mean that the patient was not ovulating, and it would be of value to know if there was any lutein tissue present at the time of operation.

The causes of follicular atresia—cystic degeneration of corpora lutea and corpora albicantia—and follicular retention cysts are different. If it can be assumed that the cysts in this case were follicular and due to non-rupture of the follicle, then the pelvic adhesions may have been a causal factor. It is considered that old pelvic infection, by thickening the tunica albuginea, interferes with ovulation, giving rise to "sclero-cystic disease" of the ovaries. No matter whether this explanation is correct, there is no doubt that cystic ovaries and pelvic adhesions are commonly associated. In the absence of some such local lesion, then failure of the follicle to rupture is assumed to be due to some disturbance of the pituitary–ovary hormone mechanism normally responsible for ovulation. The exact nature of this is still unknown, but ovulation probably requires successive and integrated action of two pituitary factors: various types of upsets in this gonadotrophic stimulus are postulated as causing cystic ovaries, but they are mainly hypothetical.

There does not appear to be any adequate reason for supposing that the ovarian condition played any part in causing the abortions, but the pelvic adhesions may have done so. Now these have been separated the chances for the next pregnancy may be better. If no other cause for the abortions can be found, the chances of the next pregnancy going to term are reasonably good. The patient should be advised to wait 6 months from the time of operation before attempting to conceive again, and when she does become pregnant should adopt the usual precautions of rest and avoidance of coitus. Vitamin E and twice-weekly injections of 5 mg. of progesterone in the early months might also be given empirically.

For the moment there is no indication to treat the cystic ovaries. They may be of little importance, and in any case may correct themselves spontaneously. If, however, the patient does not conceive again after reasonable opportunities, then premenstrual endometrial biopsy should be carried out to see if she is ovulating. If there is evidence that ovulation does not occur or is infrequent, then treatment with gonadotrophin should be tried, although it is difficult to induce ovulation in women by such means. Serum gonadotrophin (follicle-stimulating) should be given over the first half of the cycle, 400 to 1,000 I.U. intramuscularly every three days for five doses. This could be followed by injections of chorionic gonadotrophin in the second half of the cycle. As an alternative the newer preparation of gonadotrophin with synergic factor could be given. Gonadotrophic hormone therapy, however, should be used with caution, since it is reported as sometimes *causing* "cystic ovaries."

Compensation for Doctor's Illness

Q.—If a doctor is employed as a house-surgeon, R.S.O., or in any paid appointment, and contracts an illness which can be directly attributed to infection whilst acting in the hospital, is he entitled to compensation for loss of wages during his incapacity? Does the Compensation Act apply to doctors so employed?

A.—A house-surgeon or the holder of a similar appointment in a hospital is doubtless a "workman," and if his yearly salary is £420 or less he may be compensated under the Acts. He is not, however, necessarily entitled to compensation for the effects of an illness he contracts in the course of his duty. The decided cases make the law very obscure, but, broadly speaking, he has to show some element of accident.

Measles Prophylaxis

Q.—Will whole-blood taken from a parent who had measles in childhood, and given intramuscularly—e.g., into the buttock—to an infant of 18 months at the 6th day after contact, materially abate the subsequent development of measles? What dosage should be employed? Has some statistical or experimental evidence already been published in support of the above procedure?

A.—Pooled adult serum has been used on a large scale for the prevention or attenuation of measles, and a careful statistical analysis of the results obtained in over 1,000 cases is to be found in the fifth L.C.C. report on measles, published in 1938. The dosage of adult serum recommended there is in c.cm. the age of the child multiplied by 4. Thus for this child of 1½ years the dose of adult serum (to be given intramuscularly) would be 6 c.cm., or if whole blood is given, 12 c.cm. Complete protection against measles cannot be guaranteed with adult serum, but does in fact occur in 60 to 75% of inoculated contacts, with attenuation in most of the remainder. Children are most susceptible to measles at ages 1 to 3 years, and complete protection at that age could probably be obtained by a rather larger dose—say, 20 c.cm. of whole parental blood. The time after exposure when the blood or serum is given does not greatly matter up to 6 days, but after that time the chances of obtaining complete protection are lessened. Protection should, of course, be the aim in children under 2 years, but in older, healthy children attenuation is preferable, as the child with modified measles is usually immune to further attack, whereas the "protected" child is not. Modification is best obtained by giving half the appropriate dose used for protection within the first 6 days of exposure. Adult serum for use in measles contacts may be obtained in many areas through the local M.O.H.

Psychiatry in the Services

Q.—As medical officers on the Western front, we would appreciate a practical and simple explanation of the differences between: (1) anxiety neurosis, (2) hysteria, (3) battle fatigue, (4) lack of moral fibre. The differences seem tenuous, but the methods of disposal between the first three and the last vary.

A.—This is a difficult request to meet. To give an adequate explanation would demand a series of lectures covering most of the field of the psychoneuroses. We cannot expect in psychiatry such clear dividing lines as we find in "organic" medicine; the various syndromes tend to merge into one another, and "mixed states" are common. The main difficulty, however, about this list of four diagnoses is that it is a mixed classification. The names of (1) and (2) imply criteria of symptomatology and psychopathology, and the name of (3) refers to symptoms and aetiology; (4), on the other hand, is essentially a moral judgment.

The term "anxiety neurosis" is applied nowadays to an uncontrollably anxious frame of mind, recognized by the patient as excessive for the circumstances, and usually associated with lack of concentration, easy fatigability, and impairment of sleep and appetite, with physical concomitants such as tachycardia, gross sweating, etc. A case of anxiety neurosis may have a superadded hysterical symptom, but the diagnosis "hysteria" is usually confined to men who, because of the nature of their special type of basic personality, under stress convert all, or almost all, their anxiety into "functional" symptoms such as blindness, deafness, aphonia, stammer, headache, or paralysis of a limb, their conscious state of mind remaining unanxious or even nonchalant.

The term "battle fatigue" is a convenient one to use in the case of men of good physique and good previous morale who, under the long-continued stress of exposure to danger, overwork, and insufficient sleep, gradually develop a state of anxious weariness that

gives the general impression of being due to mental and physical exhaustion. Such men sometimes have to be ordered to "go sick" before they will do so. It is characteristic of them that, if free from severe depression and if given, at an early enough stage, a period off work with good food, full rest, and adequate sedation, they quickly make a good (or fair) recovery, and willingly return to duty.

Psychiatry, of course, includes within its field not only signs and symptoms in the ordinary sense but all acts of behaviour and attitudes of mind; it attempts objectively to work out the causation of the acts and to assess the significance of the attitudes. The same behaviour and attitudes can be assessed by other criteria, such as their compatibility with the immediate demands of the particular social group in which the patient finds himself at the relevant time. Such criteria loom large in wartime, and especially as regards the behaviour of men on active service. They may, in certain circumstances, be held to have overriding importance, the medical and psychiatric aspects of the case remaining true but being regarded as outweighed.

When a man is considered to be displaying unwillingness to do his duty and to be surrendering to his fear, it is sometimes said that he is showing "lack of moral fibre." The intention of the statement is presumably to keep in the foreground certain urgent practical issues, and possibly to strengthen the resolve of the men remaining on the station. The accuracy and long-term effectiveness of such a statement may by some be thought disputable. In any case, it is important to emphasize that the term "lack of moral fibre" is not a medical diagnosis. It lies outside the scientific field of medicine and psychiatry, and within the pragmatic field of military discipline. The term seems to indicate that the man in question is regarded as a coward, lacking in "guts," will power, and unselfishness; or, at least, that the circumstances demand that he be treated as such. As medical men we may be inclined to think that the patient is a hypersensitive person who more quickly than is normal develops anxiety and complains of it. We may feel that his whole life history reveals poor opportunities of developing a sense of social duty. We may find evidence that the general morale of his particular section is rather low. Possibly, it will seem that factors of all these three kinds play a part.

It would be less difficult to deal with this question if medical officers could stick to their last, reporting after examination on the *medical* aspects of the case, and leaving the use of the term "lack of moral fibre" to the executive authorities.

LETTERS, NOTES, ETC.

Sprouting Legumes

Dr. J. GEE-TSEH MAR (Manchester) writes: Bean-sprouts have been eaten by the Chinese from time immemorial, and may be found on the menus of their restaurants, even in this country. Space does not permit details, but here are a few further points from their technique. (1) Chinese green beans the size of match-heads are used. These have a moderate rate of growth, and the tiny softened cotyledons are easier to chew and digest. (2) Wooden containers retain moisture better than metal ones, so a bucket or keg is ideal. Two or three 1/2-in. holes in the bottom are sufficient for drainage, the beans being kept in by lining the bottom with a piece of matting. (3) Water twice daily with lukewarm water (in this climate), and drain well to prevent the bottom beans from rotting. (4) Cover loosely with matting or a wooden lid to prevent green leaves. Place in a warm dark place. (5) Vary the temperature of the water and surroundings according to experience. Too rapid growth produces tough, weedy shoots with long leaves, and overheating produces brownish rot. Aim at fat, stubby, succulent shoots about an inch long, and taking about a week to grow. (6) When ready, place the sprouts in a loose wire strainer, and gently swish in a basin of cold water. This separates the now black husks, leaving the snowy white shoots. Recently the American magazine *Life* printed an excellent article on methods of cooking bean-sprouts.

Use of Sulphonamide Pastilles in the Oral Cavity

Mr. HENRY J. MURPHY, M.B., B.D.S., writes from Dublin: For some years I have been using sulphonamide preparations for various conditions in the mouth. Most of the treatments are routine and known to most dentists and doctors, but there is one type of therapy from which I am getting very good results and which I think is little used. I got a pastille made up in a gelatin base containing approximately 2 grains of sulphapyridine and flavoured with menthol. After I extract teeth or do any oral operation I put the patient on these pastilles in the following way. He is to place one in his mouth and allow it to dissolve as slowly as possible (most patients can make the pastille last from half to three-quarters of an hour). I give one pastille immediately after the operation and then fit them into the daily dosage of one pastille on awaking in the morning, two at equal intervals between breakfast and lunch, two at equal intervals between lunch and dinner, one between dinner and bedtime, and one last thing at night. After a severe operation such as extraction of all the teeth I would give two extra tablets the first and second days to make the intervals shorter. I keep up this routine for four days and then reduce the dosage to four pastilles divided equally over the day. I don't syringe the sockets or advise mouth-washes, except when necessary to clear food particles out of the wounds. I find the action of these pastilles and the saliva a more perfect healing stimulus than any other treatment; pain is reduced to a minimum and healing is clean and rapid. I get no gross sepsis or dry sockets after teeth extractions. There will be some pain and swelling, but this is in relation to the trauma caused by the operation and the amount of sepsis of the teeth. I find that whatever infection is present rapidly clears up without the complication of more infection being added from mouth bacteria, and that this healing of the infected areas is as painless and rapid as the body tissues can accomplish it. Before I took to the pastilles I used to break a tablet of sulphapyridine into four equal parts; the quarter tablets gave good results but dissolved faster and therefore would not give as even a distribution of the drug as my present pastille. The dosage of the sulphonamide is big enough to combat the bacteria in the area and still not large enough to have any serious effect on the patient, such as large doses taken orally will sometimes cause.

Effects of Sexual Continence

Dr. A. D. MCDWYER (Dublin) writes: The answer to the query on the effects of sexual continence (Jan. 13, p. 67) omitted a fact which, however unfamiliar, is very pertinent to this subject. It has been demonstrated by seminal vesiculography in a series of normal males that the seminal vesicles in the absence of emissions, involuntary or otherwise, completely and gradually empty per urethram over a period of approximately 40 days (*Med. Annu.*, 1937, John Wright and Sons, Bristol). Consequently it seems that the seminal fluid is not normally retained. Secondly, a spontaneous and involuntary ejaculation during sleep is not, of necessity, a normal mechanism to prevent the retention of semen in completely continent males. Since Nature has provided for complete continence it seems illogical to impute various vague ills and psychological upsets to chastity *per se*. No ill effects result from such a state in a normal male.

Treatment of Varicose Ulcer and Eczema

Dr. R. R. FOOTE (London, W.1) writes: Under this heading (Jan. 6, p. 26) Dr. M. Ghosh does a great service in calling attention to the use of elastic web bandage as a substitute for the almost universal use of elastic adhesive bandage. His reasons for discarding the latter are that many cases are allergic to the constituents of the bandage, that haemorrhages of ulcers may occur under it, and that these bandages are, anyway, difficult to obtain. He might have quoted Dickson Wright, that it is harder to apply an elastic adhesive bandage *correctly* than it is to remove a gall-bladder! I would like to add to Dr. Ghosh's suggestions for treatment the use of crude coal tar for his eczematous cases, the application of Unna's plasters according to the technique of Dickson Wright, and the use of the "ceraban" bandage. I feel that Dr. Ghosh's 100% success with 112 cases would not remain at this high level unless he availed himself of these suggestions.

Oxalated Blood for Cell Counts

Dr. G. J. W. OLLERENSHAW (Sunbury-on-Thames) writes: I would like to support Dr. Martin Folan's letter (Jan. 13, p. 70) with regard to the use of oxalated blood specimens for cell counts. In my experience one can obtain a very high degree of accuracy (as compared with specimens collected at the same time and counted immediately without the addition of an anticoagulant), provided the oxalated specimen is examined within 24 hours of collection. As Dr. Folan points out, if a smear is made when the blood is collected a full blood count can be performed. The quantities used in this work here are 3 c.cm. of venous blood with the addition of 0.5 c.cm. of the following mixture: 1.2 g. ammonium oxalate; 0.8 g. potassium oxalate; 100 c.cm. distilled water, with the addition of 1 c.cm. 40% formalin. We are about to introduce a modification, which should be even more satisfactory, by drying this solution on to the walls of the specimen tube in an oven prior to dispatch.

Infected Foci in Blood-stream Infections

Dr. SYDNEY PERN (Ballarat, Victoria) writes: The *Journal* for Sept. 16, 1944 (p. 380), contains a reference to penicillin in bacterial endocarditis. It also mentions that in spite of the blood becoming sterile the patient relapsed. I would like to make the following suggestions. In blood-stream infections the micro-organisms have to gain entrance from some site—such as tonsils, infected sinuses, pyorrhoea, apical abscesses, etc.—and just so long as these infected foci are left so will the organisms continue to invade the blood stream. It is a very moot point if organisms are able to breed and multiply in the blood stream, so the obvious conclusion is that they are pouring in from outside. I have not yet heard of anybody attempting to remove any of the foci of infection in these desperate cases, yet it would appear the most logical procedure to adopt. I hope that somebody will have the temerity to try.